

A Collection of

NIDA NOTES

NATIONAL INSTITUTE
ON DRUG ABUSE

Articles That Address



DRUGS
AND
AIDS

U.S. Department of Health and Human Services
National Institutes of Health
National Institute on Drug Abuse

NN0012

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Introduction

The National Institute on Drug Abuse (NIDA) supports most of the world's research on drug abuse and addiction. NIDA-funded research enables scientists to apply the most advanced techniques available to the study of every aspect of drug abuse, including:

- genetic and social determinants of vulnerability and response to drugs;
- short- and long-term effects of drugs on the brain, including addiction;
- other health and social impacts of drug abuse, including infectious diseases and economic costs;
- development and testing of medication and behavioral treatments for abuse and addiction; and
- development and evaluation of effective messages to deter young people, in particular, from abusing drugs.

Included in this document are selections of topic-specific articles reprinted from NIDA's research newsletter, *NIDA NOTES*. Six times per year, *NIDA NOTES* reports on important highlights from NIDA-sponsored research, in a format that specialists and lay readers alike can read and put to use. Selections like the current one are intended to remind regular *NIDA NOTES* readers and inform other readers of important research discoveries during the periods they cover.

We hope the information contained here answers your needs and interests. To subscribe to *NIDA NOTES* and for further information on NIDA's drug abuse and addiction research, please visit our Web site at www.drugabuse.gov.

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Selenium Shows Promise as an Adjunct Therapy for HIV



Daily selenium supplements could serve as a useful adjunct therapy for HIV infection by holding HIV-1 viral load in check and elevating levels of infection-fighting CD4 cells. A randomized controlled trial, led by Dr. Barry Hurwitz of the University of Miami, included 262 HIV-infected men and women. After 9 months of treatment, greater increases of serum selenium predicted lower HIV viral load and greater CD4 cell count. Notably, of the 141 selenium-treated participants, the 50 whose selenium levels increased by 26.1 mg/L or more displayed no increase in HIV viral load, and their concentrations of CD4 cells increased by 24.2 percent. In contrast, the 121 placebo-treated participants averaged an increase of 20.2 percent in HIV viral load, which researchers consider large enough to affect the course of the disease. The selenium-treatment advantage, which was gained

only by participants who took the supplement as scheduled, held when the researchers accounted for factors that affect immune responses, including antiretroviral therapy. No side effects were observed.

Source

- *Archives of Internal Medicine* 167(2):148-154, 2007. **NN**

Morphine Speeds AIDS Onset in Monkeys

Dr. Anil Kumar and colleagues at the Ponce School of Medicine, Puerto Rico, have discovered key ways in which morphine may accelerate the progression of AIDS: The drug increases both viral replication and alterations in a particular part of the virus's coating. Monkeys exposed to long-term morphine administration—20 weeks prior to infection with simian/human immunodeficiency virus (SIV/SHIV) and throughout the 56-week study period—progressed to AIDS faster and showed more signs of compromised immune systems than comparison animals. Of the morphine-exposed animals that developed AIDS, three demonstrated higher viral replication in their blood and cerebrospinal fluid (CSF). When the researchers zeroed in on particular areas of the viral envelope—a lipid-protein covering that helps viruses penetrate cells—they found that morphine-exposed monkeys demonstrated a higher degree of change in the V4 region than control animals. This difference, which may expand the range of cells that HIV can infect, occurred in both CSF and blood. The extent of V4 evolution corresponded with rapid disease progression. Studies such as this aim to open new avenues for intervening against HIV.

Sources

- *Virology* 354(1):192-206, 2006.
- *Virology* 358(2):373-383, 2007. **NN**

Researchers Report on Progress of NIDA's Southern Africa Initiative

Research projects conducted under NIDA's Southern Africa Initiative help universities and other organizations in southern Africa build research capacity and infrastructure in the area of addiction, particularly drug-related HIV transmission. The Initiative, administered by NIDA's Special Populations Office (SPO) with assistance from the International Program, comprises 12 research projects. NIDA-funded investigators based in the United States and African collaborators recently reported on the progress of their projects, most of which have taken place or are ongoing in the Republic of South Africa.

Dr. Torrance Stephens of Morehouse School of Medicine and Dr. Sibusiso Sifunda of the South African Medical Research Council described the development and testing of a peer-led intervention to prevent about-to-be-released prison inmates from spreading sexually transmitted diseases, including HIV, to community residents. The intervention—which included cultural perspectives on manhood and responsibility, videotaped stories from role models, and group discussions—improved participants' attitudes regarding safe sex and their motivation to reduce risky behaviors. The research team worked closely with the South African minister of corrections and the Department of Correctional Services (DCS) in nine provinces and four prisons to provide training for DCS staff and peer education for ex-inmates.

Dr. Murelle Harrison of Southern University in Baton Rouge, Louisiana and Dr. Dorothy Malaka of the University of Limpopo, South Africa, reported on a comparison of African-American and South African families living in rural areas. They observed similar sociodemographic and family characteristics and youth behaviors in both populations. For example, children who spent more time interacting with their mothers also showed

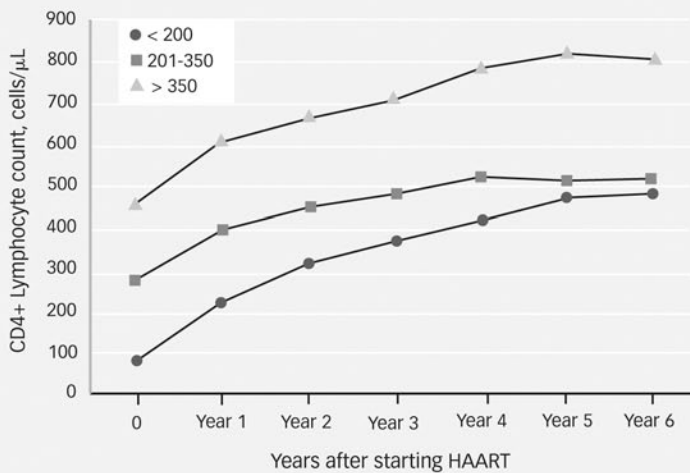
better self-control and cognitive development. The team hopes the baseline data will serve as a foundation for a subsequent family intervention. In other project results, 22 South African students were trained in epidemiological data collection methods, two South African researchers observed rural data collection in the United States and sharpened skills with computer software for data analysis, and 18 primary school teachers and nine principals received assistance with educational computer technology.

Dr. Donnie Watson of the Friends Research Institute in Torrance, California and Dr. Solomon Rataemane of the University of Limpopo reviewed preliminary findings from a comparison of three different approaches to teaching experienced drug abuse counselors cognitive-behavioral therapy: (1) in-person training with subsequent supervision, (2) distance learning of the same training with subsequent telephone-based supervision, and (3) self-study with a therapy manual after an initial orientation. The in-person and distance-learning approaches were well-received, and the team continues to recruit licensed clinicians who work in 30 South African National Council on Alcoholism and Drug Dependence treatment centers.

“The Southern Africa Initiative represents a relatively small investment, \$2 to \$2.5 million, with a tremendous payoff for all participants,” says SPO Chief Dr. Lula Beatty. “After hearing reports on the research projects, my colleagues and I were struck by the immediate impact that some of the collaborations had on communities.” NIDA hopes that information obtained from the projects will facilitate the use of evidence-based interventions that are culturally appropriate for southern Africa and that the training activities will strengthen addiction research in the region. **NN**

HIV Patients Show Better Immune Recovery With Early Initiation of HAART

WHAT THE NUMBERS SAY



Among 655 men and women with HIV, CD4+ count at HAART initiation predicted subsequent recovery of this important immune system cell. Patients receiving HAART showed an improvement after 4 years of treatment and maintained these levels for the next two. The researchers note, however, that those who began treatment after their CD4+ levels fell below 350 cells/μL failed to recover to normal levels. To achieve better recovery, the authors suggest that HAART therapy be initiated when the CD4+ cell count is greater than 350 cells/μL.

SOURCE: Moore, R.D. and Keruly, J.C. CD4+ cell count 6 years after commencement of highly active antiretroviral therapy in persons with sustained virologic suppression. *Clinical Infectious Diseases* 44(3):441-446, 2007.

Meeting Reviews Roles of Drug Abuse and Risky Behavior in HIV



More than 400 researchers and clinicians gathered in Bethesda, Maryland, May 8-9 to discuss the impact of drug abuse on the spread of HIV. NIDA sponsored the meeting in collaboration with other National Institutes of Health agencies and the Centers for Disease Control and Prevention.

Drug and alcohol abuse can prompt poor judgment and actions that people might not engage in otherwise, for example, risky sexual behaviors with infected partners. Drug abuse also may increase HIV transmission when abusers trade sex for drugs or money. The increased risk of HIV related to drug abuse extends beyond the sharing of drug injection equipment to include such risky behaviors.

Dr. Igor Grant of the University of California, San Diego, addressed methamphetamine abuse and HIV. The drug and the infection each cause degenerative brain disease. They may damage neural tissue through a common biological pathway—for example, enhanced inflammatory responses—but also seem to generate distinct pathologies that may combine to exacerbate each other. The resulting cognitive impairments may explain why methamphetamine abuse reduces adherence to HIV medications, that, in turn, may facilitate HIV transmission.

Dr. Jonathan M. Ellen of the Johns Hopkins University School of Medicine linked marijuana abuse with risky sexual behavior among African-American youth in San Francisco. Another study indicated that HIV-infected young women who abuse marijuana are less likely to keep medical appointments. Dr. Richard A. Rawson of the University of California, Los Angeles, reported preliminary results suggesting that addiction treatment reduced risky sexual behaviors among methamphetamine abusers—adding to similar findings among methamphetamine-abusing men who have sex with men (see

“Treatment Curbs Methamphetamine Abuse Among Gay and Bisexual Men,” *NIDA Notes*, Vol. 20, No. 4) Similarly, Dr. Kenzie L. Preston of NIDA’s Intramural Research Program reported that adding behavioral therapy to methadone maintenance treatment can reduce risky behaviors among outpatients addicted to heroin and cocaine.

NIDA-funded research on the link between drug abuse and HIV infection extends to the international community. Dr. Steffanie A. Strathdee, an infectious disease epidemiologist at the University of California, San Diego, reported that HIV infection among injection drug users has risen sharply in many countries—including the Ukraine, the Russian Federation, Vietnam, Iran, and China—with emerging epidemics in other nations. Interventions that reduce risky behaviors among populations that interact with both high- and low-risk individuals (for example, prisoners, non-injecting drug users, and sex workers who inject drugs) are important opportunities for HIV prevention.

Participants also discussed the disproportionate burden of HIV/AIDS among people in prisons and jails and the importance of interventions in such settings. Improved technology now allows for faster HIV testing, and expanded testing and counseling are key components of prevention strategies for drug abusers and other groups.


Adolescent Inhalant Use Is Stable Overall, but Rising Among Girls

Almost 5 percent of girls between the ages of 12 and 17 used an inhalant to get high in 2005, an increase from 4.1 percent in 2002, according to a new report. Overall, inhalant use by boys and girls in this age group remained stable over the 4-year period, at an average annual rate of 4.5 percent, or an estimated 1.1 million adolescents.

The report, “Patterns and Trends in Inhalant Use by Adolescent Males and Females: 2002-2005,” is based on an analysis of the 2002-2005 National Household Survey on Drug Use and Health, an annual survey sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA). SAMHSA, NIDA, and other federal agencies released the report at a March 15 press conference to kick off the 15th National Inhalants and Poisons Awareness Week, March 18-25.

“Young people who turn to inhalants may be completely unaware of the serious health risks,” said NIDA Deputy Director Dr. Timothy P. Condon. “We know that inhalant abuse can start early, with research suggesting that even preadolescent children seek them out because they are easy to obtain. NIDA research also indicates that those

who begin using inhalants at an early age are more likely to become dependent on them—and long-term inhalant abusers are among the most difficult drug abuse patients to treat.”

The report is available at www.drugabusestatistics.samhsa.gov/2k7/inhalants/inhalants.pdf. 

Journal Highlights Global Nexus of Drug Abuse and HIV/AIDS

One of the most urgent public health goals of addiction researchers is to curb drug abuse behaviors that contribute to the spread of HIV/AIDS, says a special supplement to *Drug and Alcohol Dependence* sponsored by the NIDA International Program.

Dr. Steven Gust, director of the program and an editor of the supplement, observes that about 5 percent of the world's population aged 15 to 64 abuses drugs and that this behavior is a major factor in the transmission of HIV/AIDS and other illnesses. Two key routes of HIV infection are through the sharing of needles and other drug injection paraphernalia and high-risk sexual contact, with the latter being one of the fastest-growing routes among women.

NIDA-supported research has shown that preventive interventions and substance abuse treatment can reduce the transmission of HIV in drug-abusing populations. By promoting collaborative research across the globe, the NIDA International Program hopes to improve treatments and outreach programs to reduce high-risk drug use and sexual behaviors, Dr. Gust says.

The supplement compiles studies—several of them funded by NIDA—on drug-related HIV transmission in 16 different localities across the globe. Most of the studies focus on injection drug use, a primary pathway for HIV transmission. Some of the topics covered are:

- The relationships between needle-sharing practices and HIV infection among heroin abusers in Dar es Salaam, Tanzania;
- The prevalence of HIV and hepatitis C infections among injection drug users receiving substance abuse treatment in two large hospitals in Barcelona, Spain;

- HIV prevalence among heroin-addicted individuals in Muar, Malaysia;
- Sexual risk behaviors among injection drug users in Shanghai, China;
- The impact of drug abuse on adherence to highly active antiretroviral therapy (HAART) among HIV-positive outpatients in France;
- HIV/AIDS risk factors along the U.S.-Mexico border;
- Regional differences in the characteristics of injection drug users in New South Wales, Australia; and
- The acceptability of audio computer-assisted self-interview among substance abusers in Rio de Janeiro, Brazil.

Since 1990, the NIDA International Program has fostered cooperative research and the exchange of scientific information by drug abuse researchers worldwide. The program's objectives include promoting international research and collaboration, communicating and disseminating science-based drug abuse information, and supporting research training and exchange opportunities. More information on the link between drug abuse and HIV/AIDS is available at www.hiv.drugabuse.gov.

Source

- Gust, S.W., Strathdee, S.A., and Winstanley, E.L., eds.. Drug Abuse and HIV/AIDS: International Research Lessons and Imperatives. *Drug and Alcohol Dependence* 82(S1), 2006. **NN**

Challenges in HIV/AIDS Research

By NIDA Director Nora D. Volkow, M.D.

The HIV/AIDS epidemic has always been a moving target for health and prevention planners, with infection rates rising in some population groups as they level off or fall in others. Recently, the disease has spread most rapidly among women, minorities, lower income groups, and young men who have sex with men (MSM). Of particular concern to NIDA are the heavy burden of HIV among African-Americans and the growing importance of heterosexual activity associated with drug use as a source of viral transmission. To elucidate the current dynamics, NIDA has developed two new initiatives: Health Disparities in HIV/AIDS: Focus on African Americans (PA-06-069) and Non-injection Drug Abuse and HIV/AIDS (PAS-06-054).



African-Americans: Higher Prevalence, Worse Prognosis

People from all racial and cultural backgrounds contract HIV/AIDS, but in the United States, African-Americans carry a disproportionate burden of the disease. Although they make up only 12 percent of the U.S. population, African-Americans accounted for half of the new AIDS cases diagnosed in 2003. Of persons diagnosed with AIDS since 1995, a smaller percentage of African-Americans (60 percent) than Whites (70 percent) were alive 9 years after diagnosis. NIDA-supported investigators have identified some contributing factors:

- A higher likelihood that a particular episode of sexual activity or injection drug abuse will result in HIV transmission among African-Americans than other ethnic groups: The elevated prevalence of HIV in the African-American community raises the chances that a sexual or needle-sharing partner will have the virus.
- Lack of awareness of HIV status: African-Americans account for more than half of those receiving an AIDS diagnosis within 1 year of testing positive for

HIV, an indication that the infection went undiagnosed for a long time. A related finding suggests that as many as 90 percent of African-American HIV-positive MSM do not know they are infected.

NIDA's African-American initiative will support research to further illuminate the causes of the HIV disparities affecting African-Americans, as well as research on:

- Access to HIV treatment and services available to drug-abusing African-Americans;
- Connections between HIV/AIDS and criminal justice involvement;
- Mental health issues that influence HIV high-risk behaviors; and
- Sociocultural factors that enhance, sustain, or perpetuate health disparities.

Noninjection Drug Use and HIV/AIDS

Since the early years of the epidemic, NIDA-supported research contributed to a decline in the proportion of HIV/AIDS cases attributable to injection drug use. Now, NIDA is also focusing attention on ways that noninjection drug use—more prevalent by far—may contribute to new HIV infections. We know that drug abuse affects judgment and may lead to high-risk sexual encounters that increase transmission rates. There also is evidence that, regardless of the route of exposure, drugs have immunological effects that may increase the risk of HIV transmission and disease sequelae. To further advance scientific understanding of the relationships, we support studies that help explain how, where, why, and among whom HIV/AIDS is spreading through noninjection drug use and associated high-risk sexual behavior; and studies that develop effective prevention and treatment interventions. **NN**

Methamphetamine Increases, and HIV Decreases, Brain Volumes

HIV infection and methamphetamine addiction produce distinct, partly overlapping effects on brain structures.

By John S. DeMott, *NIDA NOTES* Contributing Writer

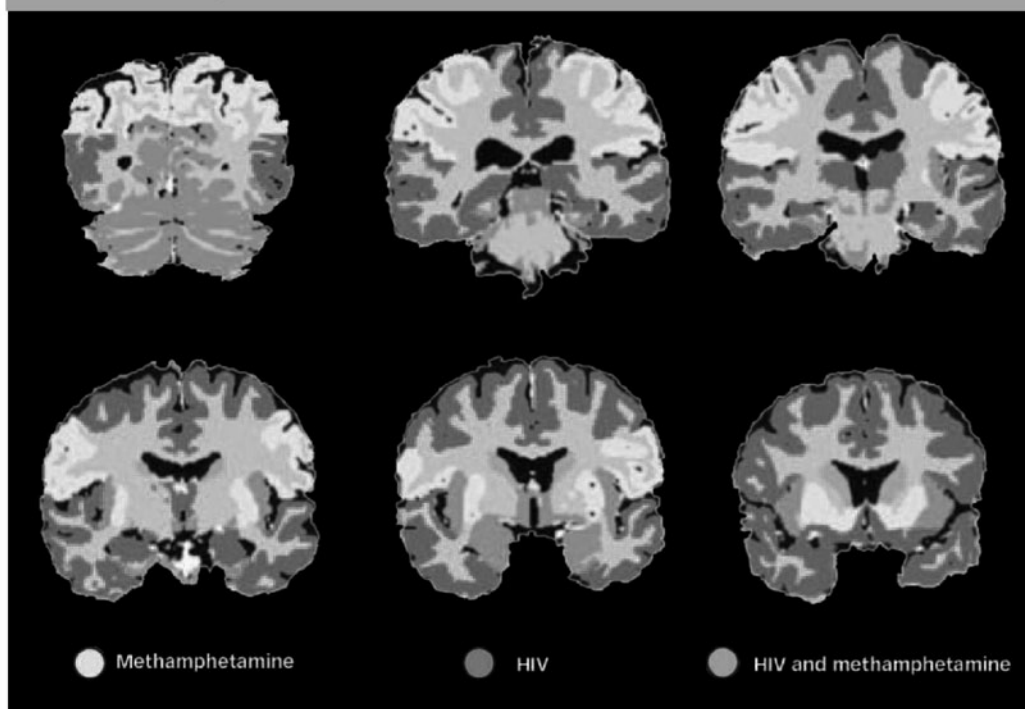
In a study that confirmed the association between HIV infection and loss of brain volume, NIDA-funded investigators also found an association between methamphetamine addiction and increased regional brain volume. Each type of volume change was associated with neurocognitive impairments, but it was unclear whether the two together caused any cognitive effects beyond the sum of what each produced individually.

Using structural magnetic resonance imaging (MRI), Drs. Terry L. Jernigan, Anthony C. Gamst, and colleagues at the University of California, San Diego (UCSD) mapped the major gray-matter brain structures of 103 people in four age- and education-matched groups: HIV-infected; methamphetamine-addicted; having both conditions; and having neither. The methamphetamine-addicted individuals were in recovery at UCSD's HIV Neurobehavioral Research Center.

After accounting for normal age-related reductions in brain volume, the participants with HIV had smaller volumes of cortical, limbic, and striatal structures, with the associations being most pronounced in the frontal and temporal lobes. Methamphetamine addiction was linked with increased volume in the parietal cortex and in all three segments of the basal ganglia—caudate nucleus, lenticular nucleus, and nucleus accumbens (NAc). In the caudate, volume reductions related to HIV and increases related to methamphetamine overlapped, producing a net volume approximating normal.

A further analysis of the volume data may reinforce existing evidence that drug abuse is especially damaging during adolescence and young adulthood, when the brain is still developing. The results showed that addicted individuals who were younger had greater NAc volume differentials compared with their non-drug-abusing age mates than did older addicted individuals. One possible explanation for this is that the drug interfered with the pruning of some NAc connecting fibers that normally occurs in the transition to adulthood, producing a small but measurable reduction in NAc volume. "While we can't be certain of the explanation, this finding highlights the concern that

HIV SHRINKS BRAIN VOLUME, METHAMPHETAMINE ABUSE INCREASES IT Composite magnetic resonance imaging (MRI) scans of brain cross-sections show the effects of methamphetamine abuse and HIV infection on brain architecture. Volumes of regions shown in yellow were larger in methamphetamine-addicted individuals than in unexposed controls. Volumes of regions shown in red were smaller in HIV-positive than in noninfected individuals. The volume in the caudate nucleus, shown in orange, illustrates the superimposed effects of both conditions, which had an offsetting effect on volume. The offsetting volume effect did not cancel the functional brain damage associated with HIV infection and methamphetamine abuse.



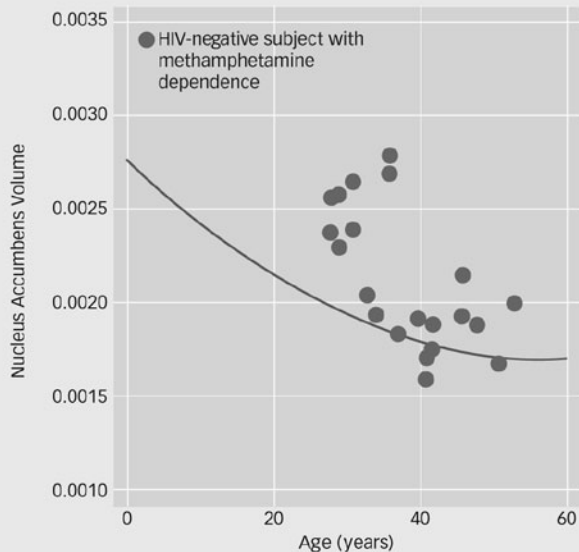
Reprinted from *American Journal of Psychiatry*, Vol. 162(8):1461-1472, Jernigan, T.L., et al.: "Effects of methamphetamine dependence and HIV infection on cerebral morphology," © 2005, with permission from the American Psychiatric Association.

exposure during adolescence may alter the course of ongoing brain maturation,” says Dr. Jernigan (see chart).

Although the study results provided little information about specific drug mechanisms, the investigators note that animal studies have shown methamphetamine can incite inflammatory responses and abnormal growth of nerve fibers, each of which can increase tissue volume. “These findings emphasize that the brain’s response to stimulant exposure, and indeed to HIV as well, is probably quite dynamic, characterized by overlapping responses in different glial, as well as neuronal, cell populations,” says Dr. Jernigan. “The findings raise interesting questions for multiple-modality imaging studies, and underscore the degree of neural plasticity, and thus the potential for targeted intervention.”

Dr. Jernigan says a finding of extensive change in the parietal cortex of methamphetamine abusers “helps to confirm the importance of parietal lobe involvement and may help correct a tendency in the field to neglect this region.”

NAC VOLUME DROPS WITH AGE, INCREASES WITH METHAMPHETAMINE ABUSE The volume of the nucleus accumbens (NAC) normally decreases with age, but this process appears to have been attenuated in younger methamphetamine-addicted subjects. Abusers in their 20s and 30s had average NAC volumes resembling those of drug-free 10- to 15-year-olds.



The healthy comparison curve is shown.

Reprinted from *American Journal of Psychiatry*, Vol. 162(8): 1461-1472, Jernigan, T.L., et al.: “Effects of methamphetamine dependence and HIV infection on cerebral morphology,” © 2005, with permission from the American Psychiatric Association.

“The fact that brain alterations in methamphetamine dependence and HIV infection are distinct from each other is a clue that may help us to sort out the origins of different kinds of mental problems in these individuals.”

Implications for Brain Function

The researchers looked for correlations between the brain volume abnormalities and ratings of neuropsychological impairment. At the outset of the study, all other groups were significantly impaired relative to the HIV-negative and methamphetamine-negative group, which had a rating of 2.9 compared with 4.7 for those with both conditions, 4.2 for methamphetamine-addicted participants and 4.1 for HIV-positive individuals. Brain impairment was most pronounced in the HIV-positive participants with the most extensive loss of cortical volume and in the methamphetamine-addicted participants with the highest increase in cortical volume. The investigators found only one significant correlation between brain volumes and impairment in addicted individuals with HIV, a finding they believe probably reflects confounding by the opposed volume impacts of the two pathologies. The correlation was between hippocampal volume—a structure that both factors may damage—and severity of cognitive impairment in the dually diagnosed group.

“The fact that brain alterations in methamphetamine dependence and HIV infection are distinct from each other is a clue that may help us to sort out the origins of different kinds of mental problems in these individuals,” Dr. Jernigan says. “This is very exciting, because our results raise a number of specific questions that may not have been posed without these findings.”

Dr. Ro Nemeth-Coslett, a NIDA psychologist, agrees. “As often happens in research, these results raise more questions than they answer. Dr. Jernigan’s findings of structural inconsistencies in pathology are unaccounted for. Now we need mechanistic studies to provide a clearer understanding of what aspects of microscopic cellular organization actually drive the MRI measures.”

Source

- Jernigan, T. L., et al. Effects of methamphetamine dependence and HIV infection on cerebral morphology. *American Journal of Psychiatry* 162(8):1461-1472, 2005. **NN**

Cocaine Abuse and HIV Are Linked With Coronary Calcification

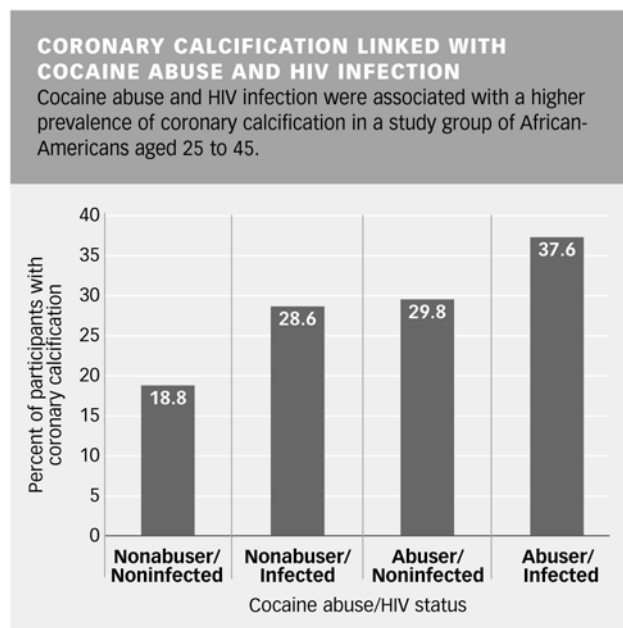
Cardiovascular changes that are potential risk factors for serious heart disease are detected in relatively young people with HIV infection or a history of cocaine abuse.

By Lori Whitten, NIDA NOTES Staff Writer

Cocaine abuse and HIV infection each raise the likelihood that calcium deposits will form in coronary arteries, according to a NIDA-supported study. The findings, by Dr. Shenghan Lai and colleagues at The Johns Hopkins University, suggest that individuals with either problem may develop elevated risks for serious, potentially fatal heart disease. The gradual buildup of calcium deposits and fat along the inner walls of blood vessels produces atherosclerosis, the narrowing and obstruction of the vessels that is a major cause of strokes and heart attacks. Although none of the participants in the study had a clinical heart problem, all were relatively young to have coronary calcification.

Dr. Lai and his colleagues used cardiac computed tomography (CT) scanning to detect the presence of coronary calcification and the number, size, and volume of calcium deposits in 192 African-American men and women aged 25 to 45. Thirty-two of the participants did not have HIV infection and had never abused cocaine (HIV-/cocaine-), 28 had the infection and were nonabusers (HIV+/cocaine-), 47 did not have the infection and had abused cocaine (HIV-/cocaine+), and 85 had both conditions (HIV+/cocaine+). About two-thirds were men.

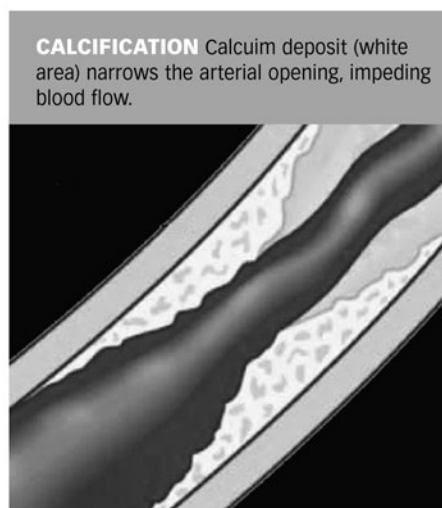
The results revealed coronary calcification in almost one-third (31 percent) of the participants. The prevalence was twice as high in the HIV+/cocaine+ group (38 percent) as in the HIV-/cocaine- group (19 percent). In the other two groups, the proportion of participants with the condition fell in between, with 29 percent of the HIV+/cocaine- and 30 percent of the HIV-/cocaine+ groups showing coronary



calcification (see chart). In the U.S. population as a whole, the prevalence of coronary calcification among 25- to 45-year-olds is about 18 percent.

Participants with HIV infection and/or a history of cocaine abuse had more calcium deposits and a greater volume of calcification than nonabusers without the infection. Compared with the HIV-/cocaine- group, the total volume of coronary calcium was 2.9 times as high in the

HIV+/cocaine- group, 2.6 times as high in the HIV-/cocaine+ group, and 3.5 times as high in the HIV+/cocaine+ group. The associations held when the researchers took into account cardiovascular disease risk factors, including age, body mass index, lipid



“Coronary calcification among people at such a young age is a striking observation and suggests that clinicians should monitor heart diseases in these populations, advise patients to make lifestyle changes, and perhaps treat conditions that affect heart health, such as high blood pressure.”

levels, blood pressure, and whether patients were taking HIV medication. The study was too small to determine whether HIV and cocaine contribute independently to calcification when both are present, or whether they interact physiologically to promote it even more.

Cardiovascular complications have been well documented in patients who abuse cocaine and also have HIV infection, but this study is the first to show arterial changes prior to the development of cardiovascular symptoms and to link them with cocaine abuse alone and HIV infection alone. Larger, longer studies are needed to confirm Dr. Lai's associations and to determine whether or how cocaine- and HIV-associated calcification progresses to clinical atherosclerosis and heart disease.

Dr. Jag Khalsa of NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse says early

signs of cardiovascular disease should be taken very seriously because they are strongly connected to two major causes of death—stroke and heart attacks. "Coronary calcification among people at such a young age is a striking observation and suggests that clinicians should monitor heart disease in these populations, advise patients to make lifestyle changes, and perhaps treat conditions that affect heart health, such as high blood pressure," says Dr. Khalsa.

Source

- Lai, S., et al. Human immunodeficiency virus 1 infection, cocaine, and coronary calcification. *Archives of Internal Medicine* 165(6):690-695, 2005. **NN**

NIDA Launches HIV/AIDS Public Awareness Campaign

The link between drug abuse and HIV infection is the focus of a new public awareness campaign launched by NIDA on November 29, 2005. NIDA Director Nora D. Volkow, M.D., announced the campaign and screened “Text Message,” a new public service announcement (PSA) aimed at teenagers, during a press conference at the National Press Club in Washington, D.C. “Drug abuse prevention is HIV prevention,” says Dr. Volkow. “In recent years, the number of young people in the United States diagnosed with AIDS rose substantially. Because drug use encourages risky behaviors that can promote HIV transmission, NIDA views drug abuse prevention and treatment as essential HIV prevention.”

The PSA shows young women text messaging on cell phones about a friend who contracted HIV after using drugs and having sex at a party. The dialogue says, “She got high, got stupid, and now she has HIV.” The announcement is being aired on television stations across the country.

The PSA was produced in collaboration with students from the Duke Ellington School of the Arts, a Washington, D.C., public high school. Students were involved in developing the concept for the PSA and also performed the lead roles. The intent is to dispel the myth that only intravenous drug abuse can lead to HIV infection and to promote awareness of the consequences of the risky sexual behavior that can follow any type of drug abuse.

“Before working on the PSA, I was more concerned about pregnancy as a result of unprotected sex than HIV infection, which seemed only to affect older people,” said Ellington student Rebecca Hollingsworth. Research has shown that this view is widespread: A large proportion of youths are not concerned about becoming infected with HIV, despite the fact that young people between the ages of 13 and 24 represent a growing percentage of new infections.



An image from NIDA's "Text Message" public service announcement

NIDA has formed a coalition with organizations including the American Academy of Child and Adolescent Psychiatry; the AIDS Alliance for Children, Youth and Families; and the United Negro College Fund Special Programs Corporation to get this important message about the link between drug abuse and HIV infection to teenagers and young adults. In addition to the PSA, which will be aired on television stations across the United States, posters advertising NIDA's message—"Drug Abuse and HIV: Learn the Link"—will be displayed on public transportation and buses in Washington, D.C., Chicago, and Dallas.

NIDA's public awareness campaign also includes a recently launched Web site, www.hiv.drugabuse.gov, where visitors can browse publications such as the new HIV/AIDS Research Report, download the PSA, and read about the latest scientific findings on the relationship between drug abuse and HIV infection. **NN**

NIDA at Work: AIDS Research Program

By Lori Whitten, NIDA NOTES Staff Writer

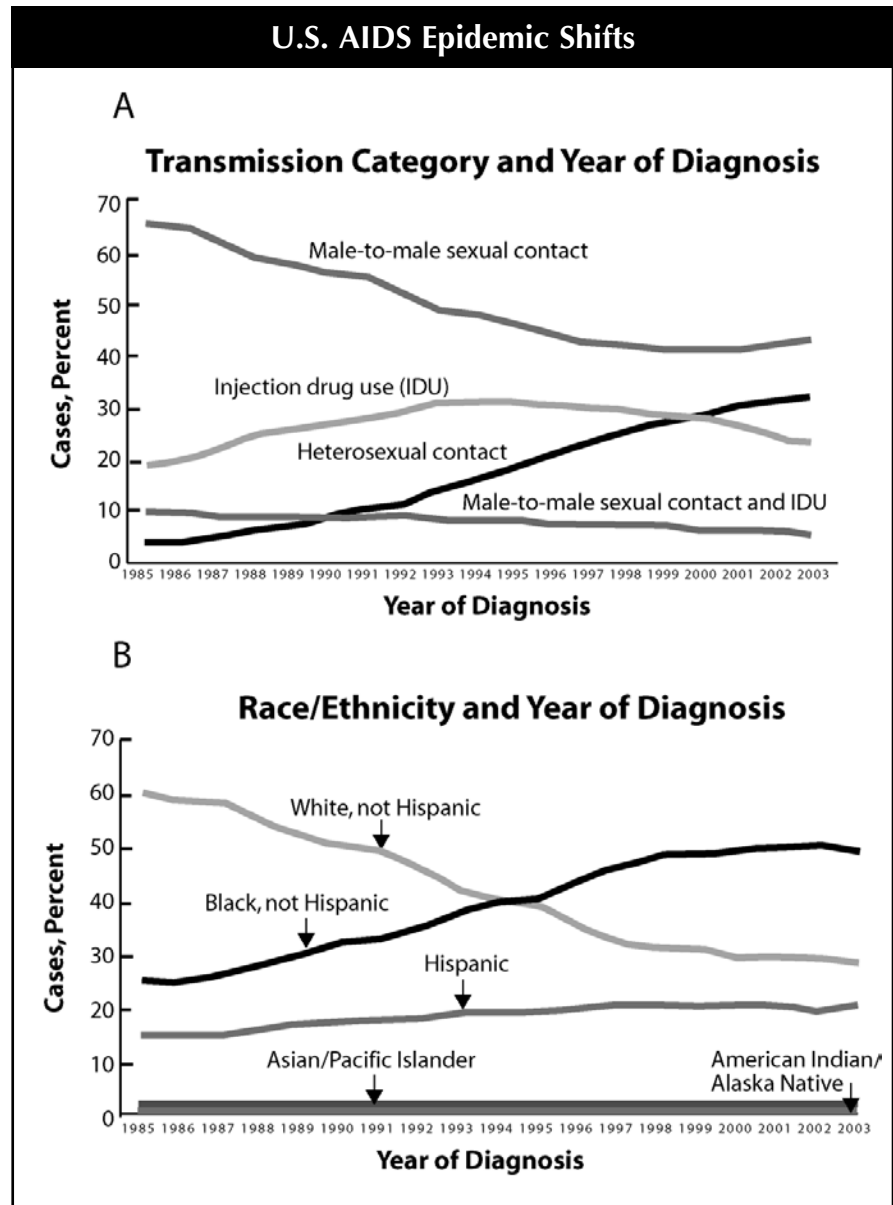
NIDA disburses more than \$275 million annually to support research on HIV and AIDS. The mandate to ensure that this investment yields the greatest possible return in new knowledge leading to more effective treatment and prevention lies with NIDA's AIDS Research Program.

Under the direction of Dr. Jacques Normand, the AIDS Research Program oversees all the Institute's HIV-related grantmaking. Dr. Normand works with three associate directors: Dr. Lynda Erinoff is in charge of planning the basic science grant portfolio; Ms. Helen Cesari manages the social science programs; and Ms. Katherine Davenny coordinates collaborative projects with other NIH Institutes and external organizations engaged in HIV/AIDS research. Every other month, the AIDS Research Program staff convenes an AIDS workgroup consisting of 20 NIDA grantmaking staff with expertise in all science areas relevant to HIV, including representatives from four Program Divisions, three Offices, the Center for Clinical Trials Network, and the International Program. In the meetings, NIDA scientists exchange up-to-date information, identify research needs and opportunities, set priorities, and look for ways to coordinate ongoing research and new initiatives.

In pursuing its mandate, the AIDS Research Program builds upon NIDA's more than 20-year history of accomplishment in HIV research. In the early 1980s, when it became apparent that injection drug use was playing a critical role in the spread of the newly recognized deadly disease, Congress identified NIDA as a key component of the Nation's response. The Institute initiated a research program that has had significant impact on the epidemic.

Along with underwriting studies leading to crucial discoveries, such as the finding that providing methadone

treatment slows the spread of the disease among injection opioid abusers, NIDA has supported the development and testing of effective science-based education, outreach, and preventive interventions for drug-abusing and other at-risk



(A) The proportion of newly diagnosed AIDS cases due to injection drug use has dropped since the 1980s, and the proportion due to heterosexual contact has increased. (B) Forty-seven percent of newly diagnosed AIDS cases in 2003 were in non-Hispanic Blacks.

populations. Partly as a result of these efforts, the number of newly diagnosed AIDS cases attributable to injection drug use in the United States dropped from 19,943 in 1995 to 6,938 in 2004.

Shifting With the Epidemic

Established in February 2005, the AIDS Research Program has come into being at a time when the character of the HIV epidemic is in transition. Since the mid-1980s, heterosexual contact—often with an injection drug user or while under the influence of drugs—has become an increasingly important route of transmission of the HIV virus. The proportion of newly diagnosed AIDS cases attributable to heterosexual contact has increased while that attributable to sexual contact among men who have sex with men and that directly attributable to injection drug use have dropped. The rise in heterosexual transmission has been especially pronounced among African Americans and women (see exhibit on the previous page, “U.S. AIDS Epidemic Shifts”).

A recent case highlights the AIDS Research Program’s role in generating efficient responses to developments in the epidemic. In February 2005, New York City public health officials reported that a new strain of HIV had been isolated from a methamphetamine-abusing man who engaged in high-risk sex with male partners. The patient responded poorly to initial treatment and progressed rapidly from infection to AIDS. The officials, worried that such a highly virulent, treatment-resistant strain might become widespread, called for heightened monitoring of treatment-resistant HIV. The AIDS Research Program and the AIDS workgroup promptly developed a plan to promote collaborations between epidemiologists, social scientists, virologists, immunologists, and infectious disease experts. Their work aims to produce a comprehensive assessment

of the potential for treatment-resistant viral strains among infected men who have sex with men and who also abuse methamphetamine.

As they realign research priorities to match the new dynamics of the epidemic, NIDA’s AIDS Research Program and the AIDS workgroup members will draw on the results of NIDA’s Sexual Acquisition and Transmission of HIV Cooperative Agreement Program (SATH-CAP). This program’s four interdisciplinary research teams are studying the patterns of viral spread from high-risk, drug-using groups to lower risk groups; for example, from drug injectors to noninjecting sexual partners, or from bisexual men to female sexual partners. Mapping these patterns will enable prevention practitioners to focus their initiatives on the social networks and activities with the most potential for containing the spread of the epidemic. SATH-CAP investigative teams are working in geographical areas where HIV is in a rapid process of bridging from one population to another. For example, one team is studying the epidemic in St. Petersburg, Russia, where the primary route of transmission is in transition from injection drug use to sexual contact.

The treatment-resistant HIV and SATH-CAP initiatives exemplify how NIDA, through the AIDS Research Program, brings the power of interdisciplinary research to bear on the intertwined problems of drug abuse and HIV/AIDS. “Interdisciplinary research among investigators with different expertise typically does not happen without coordination,” says Dr. Normand. “The AIDS Research Program is the place where NIDA ensures that its research on epidemiological, biological, and behavioral aspects of the infection among drug abusers works in concert and that knowledge from the research is translated into clinical and community practice.” **NN**

Expanded HIV Testing: Benefits May Warrant Costs

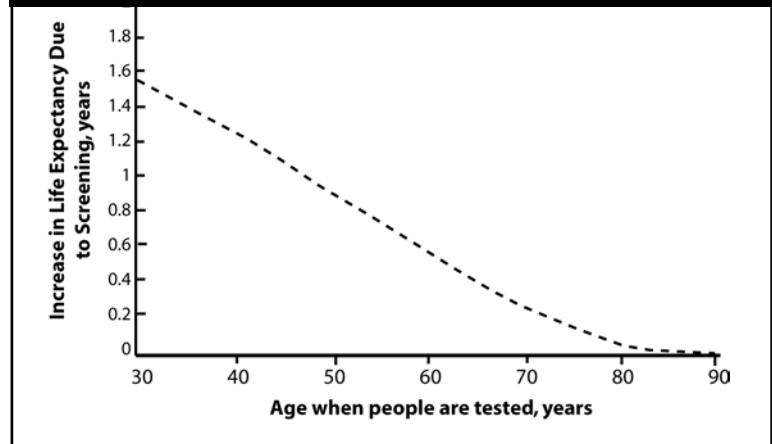
By Lori Whitten, *NIDA NOTES* Staff Writer

Offering voluntary HIV testing on a routine basis in outpatient health care settings would slow the spread of HIV and improve the survival of many of the estimated 280,000 Americans who are unaware that they are infected. The value of extending HIV screening to relatively low-risk populations in outpatient settings would be on par with the value of routine screening for other common conditions, such as colon cancer, according to two studies funded by NIDA.

In the United States, about one-quarter of the 1.04 million people estimated to be HIV infected do not know they have the virus. Under current testing guidelines, many of these individuals are likely to remain ignorant of their status for as long as they remain relatively healthy, because they do not belong to any of the high-prevalence subgroups to whom testing is recommended, and only those who live in areas with high infection rates will be screened as hospital inpatients. Meanwhile, their disease advances undiagnosed, compromising their prospects for future health and survival. They remain unaware of the need to take precautions against spreading the infection, and according to estimates from the Centers for Disease Control and Prevention (CDC), transmit the virus to 27,000 others each year.

Lead investigators in the two studies, Dr. A. David Paltiel of Yale University School of Medicine and Dr. Gillian Sanders of Duke University's Clinical Research Institute, used computer models to determine whether it would be cost-effective to extend routine voluntary screening to subpopulations with moderate prevalence of infection or to the whole population. The models use data on the estimated cost associated with an HIV test, the number of additional people who would be tested and the number of cases likely to be diagnosed sooner (and how much sooner), the greater benefits of therapy in earlier as opposed to later stages of infection, and the number of new infections that will be avoided when people who find out they are infected take precautions against transmission. Their work updates previous cost analyses by incorporating the use of state-of-the-art antiretroviral treatment (HAART) for HIV. The analyses yield estimates of the cost of each additional year of life expectancy that would be gained by expanded testing. Policymakers use such analyses to decide how to allocate funds for health.

Study Predicts Routine Voluntary HIV Testing Would Extend Survival



Compared with HIV detection based on symptoms, routine voluntary HIV testing would enhance the life expectancy of people with the infection by getting them into life-prolonging care earlier. Estimates are based on the assumption that state-of-the-art therapy would be initiated when patients had a relatively favorable CD4 count of 350 cells/m³ as opposed to 175 cells/m³, the average count associated with detection based on symptoms. The CD4 count is a measure of immune system health.

Benefits of Early Detection

Dr. Sanders, Dr. Douglas Owens of the Veterans Affairs Palo Alto Health Care System, and their colleagues analyzed a hypothetical group of patients typical of those in general health care settings. The researchers assumed the patients' average age was 43 and their rate of unknown HIV infection was 1 percent, the level at which the CDC recommends routine testing. A 1 percent prevalence of unknown infection is probably high compared with the overall U.S. population (0.1 percent), but lower than high-risk populations currently screened (3 percent). By comparing three different scenarios of HIV detection—symptom-based diagnosis, with a one-time voluntary test, and through testing every 5 years—the researchers were able to assess the lifetime benefits to patients and their partners, as well as the costs, of expanded testing.

The analysis found that one-time HIV testing would increase the life expectancies of individuals in the hypothetical population by an average of 4.7 quality-adjusted days and cost about \$15,078 for every year of life gained.

Patients whose HIV was discovered earlier and treated sooner would live on average 1.5 years longer as a result of the testing.

The \$15,078 figure assumes that earlier HIV detection would reduce the spread of infection by 20 percent. Some such reduction would be likely because once people know they have HIV, they tend to change their behavior to avoid infecting others, and when they start antiretroviral treatment their body fluids become less infectious. If transmission were not reduced, one-time HIV testing in the hypothetical population would cost \$41,736 per year of life gained—comparable to the cost-effectiveness of routine testing for colon cancer, hypertension, and type 2 diabetes. The researchers further suggested that one-time testing might be justified in terms of value in a hypothetical population with an HIV infection prevalence as low as 0.05 percent.

In the second study, Dr. Paltiel and his colleagues compared current practice with routine voluntary HIV testing

among high-risk communities (3 percent prevalence), communities with 1 percent prevalence, and the general population of the United States (0.1 percent prevalence). They estimated that adding a one-time voluntary HIV test to current care for people at high risk of infection would cost \$36,000 per life-year gained. Testing a population that meets the 1 percent threshold raises the cost to \$38,000—a figure similar to the \$41,736 estimate of Dr. Sanders and colleagues. In the high-risk population, testing every 5 years would cost \$50,000 per added life-year, rising to \$63,000 if testing were done every 3 years. The findings suggest that voluntary testing every 3 to 5 years in all populations except those with the lowest prevalence would increase survival at a comparatively attractive cost by U.S. standards, says Dr. Paltiel. A one-time voluntary screening in the general population may also be cost-effective, but merits further investigation, he adds.

“Expanding voluntary HIV testing will require an investment—but it delivers better value for money than many other chronic disease testing programs that are routinely used in the United States today,” says Dr. Paltiel. Neither research project addressed who should pay for expanded HIV screening, but the findings serve as a springboard for policy discussions involving all people with a stake in the decision. “Cost-effectiveness is just one consideration in policy decisions. Implementing expanded HIV testing also will require people believing it’s an important use of limited resources,” says Dr. Sanders.

The findings have made an impact in the state with the largest HIV caseload in the nation. Citing the research, the New York State Department of Health has revised its HIV guidelines, urging State health care providers to integrate routine testing into their medical care, use rapid HIV testing, and refer patients with positive test results to care, among other things.

“People may think of computer-based analyses as isolated and abstract, but this AIDS modeling program encourages researchers to use findings from a wide range of relevant disciplines and incorporate advice from clinicians,” says Dr. Peter Hartsock of NIDA’s Division of Epidemiology, Services and Prevention Research. “These two studies integrated data from many perspectives, and their results provide rigorous but practical information that can guide the societal discussion of what to do about the problem.”

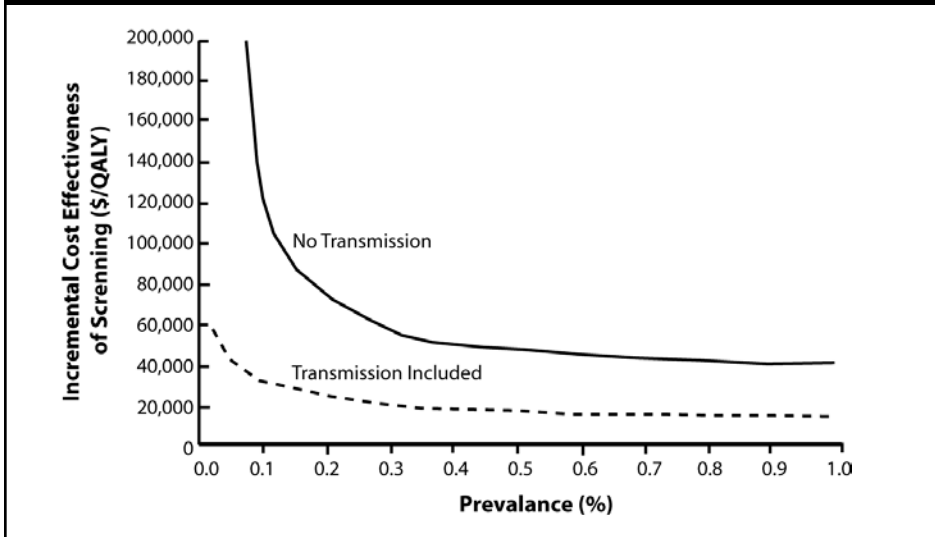
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HIV Testing and Other Routine Tests: Cost-Effectiveness Compared	
Test	\$/QALY* Gained
HIV test: All inpatients†	38,600
HIV test every 5 years: People at high risk (3% prevalence)†	50,000
HIV test one time (1% prevalence)‡ Individual benefit only	41,736
Including benefit to others	15,078
HIV test one time: U.S. general population (0.1% prevalence)†	113,000
Breast cancer test: Annual mammogram, age 50–69§	57,500
Colon cancer test: FOBT + SIG every 5 years, age 50–85§	57,700
Type 2 diabetes test: Fasting blood glucose, age >25§	70,000
Hypertension testing§	48,000
FOBT indicates fecal occult blood test; SIG, sigmoidoscopy.	
*In quality-adjusted life years (QALYs), which account for both longevity and health-related quality of life.	
†Paltiel et al (2005); ‡Sanders et al (2005); §Adapted from personal communication, Sanders and Paltiel, 2005.	

The cost-effectiveness of various HIV testing approaches compared with that of common routine tests.

Study Estimates Range of Value Associated With Routine Voluntary HIV Testing



Dr. Sanders and colleagues estimated that routine HIV testing would be relatively economical even if the prevalence rates of undiagnosed infection were as low as 0.05 percent (half that of the U.S. general population estimate) when reduced transmission to partners is considered (dashed line). Even when transmission is not considered (solid line), HIV testing might be a financially attractive option at prevalence rates well below 1 percent.

- Sanders, G.D., et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *New England Journal of Medicine* 352(6):570–585, 2005. **NN**

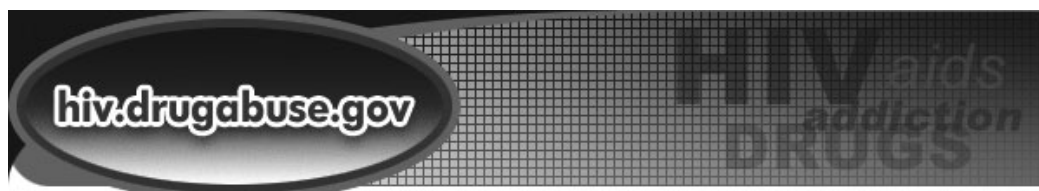
HIV/AIDS Research and Education Are Crucial to Drug Abuse Prevention

Behavior associated with drug abuse is the single largest factor in the spread of HIV infection in the United States, where about one-third of HIV/AIDS cases are related to injection drug abuse.

NIDA's Web site, <http://hiv.drugabuse.gov>, provides research-based information about HIV/AIDS and its relationship to drug abuse. A compendium of NIDA publications and public service announcements, the Web site is a valuable resource for care providers as well as parents and teens looking for information. Visitors to the site will find a list of drugs that are commonly abused, a phone number and Web site for treatment referrals, up-to-date research findings, and announcements in English and Spanish about special events.

Using or sharing drug paraphernalia such as unsterile needles, cotton swabs, rinse water, and cookers to inject heroin, cocaine, or other drugs places drug abusers at risk for contracting or transmitting HIV. Drug abuse without the use of needles and syringes can also foster the spread of HIV. Research sponsored by NIDA and the National Institute on Alcohol Abuse and Alcoholism has shown that drug and alcohol use can interfere with judgment about sexual behavior and thereby affect the likelihood of engaging in unplanned and unprotected sex. This increases the risk for contracting HIV from infected sex partners.

In the past 15 years, NIDA has sponsored a comprehensive research program in response to the dynamic nature of the co-occurring epidemics of drug abuse and HIV/AIDS. This research has yielded science-based principles that should prove useful to community planners, policymakers, service providers, and medical practitioners as they develop and implement programs to prevent the spread of HIV and



other infections among injecting and noninjecting drug users and their sexual partners. To foster widespread use of these principles, NIDA has produced a number of publications, such as *Principles of HIV/AIDS Prevention in Drug-Using Populations* and *The NIDA Community-Based Outreach Model: A Manual To Reduce the Risk of HIV and Other Blood-Borne Infections in Drug Users*.

The Web site also offers the "Jack & Jill" public service announcements, which are geared toward teens and provide information about substance abuse and risky sexual behavior. "Jack & Jill" was the first installment in NIDA's "Keep Your Body Healthy" campaign, and deals with the connection between drug abuse and contracting HIV/AIDS. It has been estimated that at least half of all new HIV infections in the United States are among people under age 25, and most of these young people are infected sexually.

NIDA's Web sites, including <http://hiv.drugabuse.gov>, help bring the Institute's research and policies to a wide audience; by disseminating material online, parents, teens, and providers have an accessible resource for the latest in drug abuse research. **NN**

AIDS Cases By Exposure Category and Sex Through 2002

Exposure category	Males		Females		Overall total	
	No.	%	No.	%	No.	%
Male-to-Male Sexual Contact	384,784	55	—	—	384,784	55
Injection Drug Abuse	151,367	22	58,552	39	209,919	30
Heterosexual Contact	36,692	5	63,379	42	100,071	14

Source: CDC. *HIV/AIDS Surveillance Report: Cases of HIV infection and AIDS in the United States, Vol. 14, 2002*. Atlanta, Georgia: U.S. Department of Health and Human Services.

Researchers Adapt HIV Risk Prevention Program for African-American Women

By Jill Schlabig Williams, NIDA NOTES Contributing Writer

The HIV/AIDS epidemic has taken a disproportionate toll on racial and ethnic minority populations, especially women. In its surveillance report on the number of Americans living with HIV/AIDS in 2002, the Centers for Disease Control and Prevention estimates that among women with HIV/AIDS, non-Hispanic African-American women outnumbered non-Hispanic white women by three to one—a racial disparity not found among men.

African-American drug-using women were addressed in two recent studies by NIDA-funded researchers in Atlanta. Dr. Claire E. Sterk of Emory University, Dr. Kirk W. Elifson of Georgia State University, and colleagues developed and tested gender-tailored, culturally specific adaptations of a standard NIDA HIV prevention intervention. They found that female African-American injecting drug users (IDUs) and crack cocaine users who

received either of two targeted 4-week prevention programs reduced their risk behaviors

related to drug-taking and sex more than did women who received the standard intervention.

“These studies are examples of research that is responsive to community needs,” says Dr. Dionne Jones of NIDA’s Center on AIDS and Other Medical Consequences of Drug Abuse. “When it comes to designing a prevention program, it’s not one-size-fits-all. You have to consider social context, be culturally sensitive and appropriate, and tailor your message to the group.”



The researchers’ goal was to develop culturally appropriate programs grounded in the reality of the daily lives of women most at risk and the difficulties they face in their individual, social, family, and sexual relations and activities. “We worked hard to develop interventions with input from this target population, deliver the interventions in a setting where they feel comfortable, and involve them in planning, implementing, and evaluating the interventions,” says Dr. Sterk.

Over 1 year, using one-on-one interviews and small focus groups, the researchers sought to define the key issues in the women’s lives and identify ways to address those issues, including such factors as gender dynamics, economic stressors, gender-specific norms and values, and power and control. Two interventions came out of this research phase. One, a motivation

Tailored Interventions Build on NIDA Intervention To Help Drug-Using Women Reduce HIV Risk

	Behavior in Past 30 days	NIDA Standard Intervention Group		Motivation Intervention Group		Negotiation Intervention Group	
		Baseline	Six-Month Followup	Baseline	Six-Month Followup	Baseline	Six-Month Followup
Injecting Drug Users	Number of days injected powder cocaine	8.2	3.1	6.4	0.1	4.7	0.2
	Number of days injected heroin	16.4	8.9	12.7	1.5	9.8	3.2
	Percentage who traded sex for drugs	70.4	40.7	50.0	20.0	42.9	10.0
Crack Cocaine Users	Mean number of days crack used	17.7	12.9	18.2	15.6	18.7	13.8
	Percentage who had vaginal sex with one or more paying partners	43.9	24.6	34.3	19.2	30.8	20.5

African-American drug-using women in three intervention groups reduced behaviors that heightened their risk of HIV infection. However, women receiving the culturally specific, gender-tailored motivation and negotiation interventions generally reported greater reductions in risky behaviors after their participation than women in the NIDA standard intervention.

intervention, was designed to motivate the participants to change their behavior. The other, a negotiation intervention, recognized that women may fear verbal or physical abuse if they propose safer sex or safer needle use and thus sought to strengthen their negotiation and conflict-resolution skills.

“Our goal in the motivation intervention was to reduce risk based on what’s realistic in the context of the participant’s life,” explains Dr. Sterk. “We worked with the women to set short- and long-term goals, celebrate successes, analyze failures, and identify and overcome barriers.” The negotiation intervention recognizes that many of the women’s challenges dealt with the need to resolve conflict and that negotiation skills are key to reducing risk.

Once the interventions were ready, more than 300 African-American women ages 18 to 59 years—68 IDUs and 265 crack cocaine users—were enrolled in the studies. All were HIV-negative and heterosexually active. The women were randomly assigned to one of the three interventions. The NIDA standard intervention was delivered in two one-on-one sessions; the motivation and negotiation interventions each involved four one-on-one sessions. (See textbox, below, for descriptions of each intervention.) At the 6-month followup, both IDUs and crack cocaine users in all three groups reported lower levels of drug-using behavior and risky sexual behaviors than they had reported before receiving the interventions. Reductions

were greater among women who received the tailored interventions.

Injecting Drug Users. The motivation and negotiation interventions were equally effective in reducing the incidence of needle and injection-works sharing. At 6 months, there was no sharing of drug injection paraphernalia in these groups; in the standard intervention group, 13 percent reported sharing needles and 18 percent reported sharing injection works. Although women in all intervention groups reduced their number of injections over time, only those in the tailored interventions reported statistically significant decreases. Participants in the motivation intervention were most likely to attend drug treatment, whereas women in the negotiation intervention reported more changes in their sexual behavior than did women in other interventions.

Crack Cocaine Users. All three interventions were associated with a drop in crack use in the 30 days preceding followup. About 40 percent of the women in each group reported no use during that period. Among those still abusing crack at followup, women in the motivation intervention were more likely to have reduced their use of crack in risky settings, such as outside or in a crack house, hotel room, or car. Women in the standard and motivation intervention groups significantly decreased the number of paying partners for vaginal sex and the frequency of sex with paying partners.

Protocols for Standard, Motivation, and Negotiation Interventions

All interventions include discussion of the local HIV epidemic, sex and drug-related risk behaviors, safer sex and drug use, and HIV risk-reduction strategies. The two tailored interventions also include a discussion of the impact of race and gender on HIV risk and protective behaviors.

The NIDA standard intervention is an HIV/AIDS education program that was developed in the early 1990s. It builds on standard HIV testing and counseling developed by CDC and adds discussion of the principles of HIV prevention for drug users and their sex partners. The intervention involves testing, counseling, and educating participants through use of cue cards on such topics as the definition of HIV/AIDS, who is at risk, and ways to reduce risk. Also offered are demonstrations on condom use and equipment-bleaching techniques for IDUs. Referrals to counseling and other services are provided.

The motivation intervention follows the format of the standard intervention for the first session but ends with asking participants to consider what they are motivated to change in their lives. During the second session, this list is reviewed and short- and long-term goals are set. The third and fourth sessions involve discussion of experiences with behavior change, including the woman’s sense of control and feelings of ambivalence about behavior change. Risk-reduction messages tailored to the participant’s level of readiness to change are also delivered in the fourth session.

The negotiation/conflict-resolution intervention also follows the NIDA standard intervention for the first session, but it ends with a discussion of intended behavior changes. The second session reviews the list of possible behavior changes and the level of control the participant believes she has and introduces general communication skills and strategies to develop assertiveness. Short-term goals are set for strengthening communication, gaining control, and developing assertiveness. Negotiation and conflict-resolution strategies are introduced during the third session and tailored to the individual during the final session.

Dr. Sterk suggests that the study's results show it may be optimal to create an intervention that combines skills taught in both the negotiation and motivation interventions. While participants in the negotiation intervention were generally more successful at reducing sexual risk behaviors, including decreasing the number of paying partners and increasing condom use with steady partners, participants in the motivation intervention had more success at changing drug-use behaviors.

Efforts were also made to assist program participants in their lives outside of the program, with success extending well beyond the study's parameters, notes Dr. Sterk. "A lot of the women who received the one-on-one support available through the tailored interventions said the program served as a re-entry into society. For example, they were encouraged to obtain a photo ID. Many reported that this simple act made them feel more connected to society again, part of the larger world." Program graduates returned to school, earned their GED, found jobs, joined the project to become counselors/interviewers, and stopped using drugs.

"Over and over, researchers are finding that we need to take a more holistic approach to intervention programs," says NIDA's Dr. Jones. "We can't just focus on drugs and sex. We must look at the big picture. It involves child-care, education, employment, housing, and job training. Community stakeholders need to develop programs that address multiple needs."

The project maintained a high retention rate—96 percent of the women enrolled in the studies completed the 6-month followup interview. Dr. Sterk attributes this success to the fact that the project was grounded in the community and to the value of involving community consultants—residents, both former drug users and others, who played key roles in recruiting, interviewing, and counseling participants.

In future research, Dr. Sterk intends to examine the cost-effectiveness of various intervention formats. "It appears that individual sessions may be more desirable

Principles That Guide Format, Content of Interventions

The interventions used by Dr. Sterk and her colleagues in this study are firmly based in theoretical research. The researchers conducted a series of one-on-one interviews and focus groups with the target population. These interviews yielded the following key principles that guided both the format and the content of the interventions.

- **Offer counseling sessions on an individual basis.** "It was very clear that women wanted to start with one-on-one sessions," says Dr. Sterk. "HIV risk behaviors involve so many private, personal issues—previous abuse experiences, actions to support their drug habits, things they'd never before discussed. They found it easier to discuss these experiences with one person, not a group."
- **Adopt a holistic approach.** Along with this research project, a clothing fair was conducted and clothes made available to program participants. Food for breakfast was provided; daycare was close by; and ongoing services, such as help preparing for job interviews, were provided.
- **Make programs community-based.** The project was headquartered in a house in the community, which was key to participants' convenience and comfort. Researchers also found it important for the women to link participation in this project to local social and health services, including local drug treatment, daycare centers, health services, and other community-based organizations. Community consultants played a key role in the project.
- **Address women's multiple social roles in the intervention.** Participants insisted that they didn't want to be labeled simply as drug users. Instead, they wanted the social context of their daily lives to be addressed, including their roles as mothers and steady partners.

and cost-effective," she predicts. Dr. Sterk would like to continue the research, assessing the long-term effects of specific interventions. She wants to develop an intervention that focuses on women's households, targeting both the woman and her main partner, and she is interested in capacity-building—translating her research into other settings and training people to develop similar programs in more communities.

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High-Risk Sex Is Main Factor in HIV Infection for Men and Women Who Inject Drugs

By Robert Mathias, NIDA NOTES Staff Writer

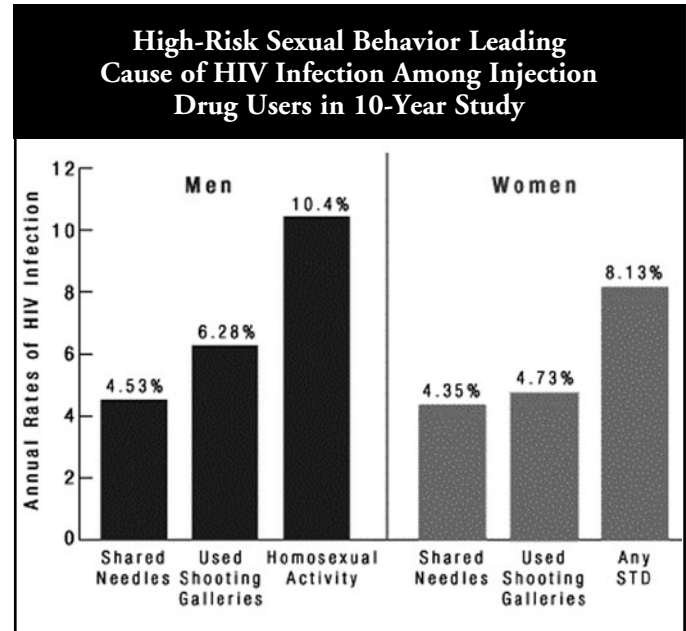
A 10-year study has found that the biggest predictor of HIV infection for both male and female injecting drug users (IDUs) is high-risk sexual behavior, not sharing needles used to inject drugs. High-risk homosexual activity was the most important factor in HIV transmission for men; high-risk heterosexual activity was most significant for women. Risky drug-use behaviors also were strong predictors of HIV transmission for men but were less significant for women, the study found.

“In the past, we assumed that IDUs who were HIV-positive had been infected with the virus through needle-sharing,” says Dr. Steffanie Strathdee of the Johns Hopkins University Bloomberg School of Public Health in Baltimore, who conducted the NIDA-funded study. “Our analysis indicates that sexual behaviors, which we thought were less important among IDUs, really carry a heavy weight in terms of risks for HIV seroconversion for both men and women.”

In the study, Dr. Strathdee led a team of researchers who analyzed data collected every 6 months from 1,800 IDUs in Baltimore from 1988 to 1998. Participants had to be at least 18 years of age when they entered the study, have a history of injection drug use within the previous 10 years, and not have HIV infection or AIDS. More than 90 percent of the participants said they had injected drugs in the 6 months prior to enrolling in the study. In their semiannual interviews, study participants reported their recent drug use and sexual behavior and submitted blood samples to determine if they had become HIV-positive since their last visit.

Researchers analyzed the role of homosexual activity in HIV seroconversions among male IDUs in the study, after taking into account other factors that increased their risk of acquiring HIV, such as their drug injection practices. This analysis revealed that the incidence of HIV infection among male IDUs who had engaged in homosexual activity within the previous 6 months was 10.44 percent a year, compared to 3.01 percent among men who did not report having homosexual sex.

Visiting “shooting galleries,” where drug abusers gather to obtain and inject drugs, sharing needles used to inject drugs with multiple partners, and injecting drugs daily also were independently linked to significantly higher rates of HIV infection among men in the study. Men who said they had used shooting galleries had an HIV incidence



High-risk sexual behavior played the biggest role in HIV infection for both male and female injection drug users (IDUs) in this study of 1,800 IDUs. Significant risk factors for men were high-risk homosexual activity, using shooting galleries, and sharing needles used to inject drugs with multiple partners. For women, high-risk heterosexual activity, as indicated by reporting a recent sexually transmitted disease (STD), was the most significant cause of HIV infection.

rate of 6.28 percent per year, and men who shared needles with more than one partner had a rate of 5.52 percent per year. These infection rates were more than double those found among men who had not engaged in these behaviors. Men who injected drugs at least once a day had HIV infection rates of 4.68 percent, more than one and one-half times the rate among men who had injected less than once a day.

Sharing needles also increased risk of HIV infection among women IDUs. However, high-risk heterosexual activity was a much more important risk factor for these women, the study found. In fact, other than being younger than 30 years—which independently predicted HIV infection for both sexes—high-risk heterosexual activity was the main predictor of HIV seroconversion among women. Women who reported having a recent sexually

transmitted disease (STD), an indicator of unprotected sex, had more than 2.5 times the rate of HIV infection of women who did not have an STD.

“Both homosexual men and heterosexual women IDUs appear to be at dual risk for becoming infected with HIV,” Dr. Strathdee says. “In previous studies by our group, being a gay male IDU was closely linked to visiting shooting galleries and sharing needles. Heterosexual women IDUs tend to have more of an overlap in their sexual partners and their drug use than men do. This puts them at increased HIV risk because they are sharing needles and having unprotected sex with a partner who is more likely to be infected with the virus.

“HIV prevention programs have done a good job in reducing needle-sharing and other drug-use behaviors that spread the virus among IDUs,” Dr. Strathdee says. “However, our study indicates that HIV prevention programs can achieve better results by also addressing sexual risk behaviors among IDUs. A multifaceted approach is needed that screens both men and women IDUs for STDs at places where they go, such as needle-exchange programs and methadone treatment programs, and provides comprehensive treatment at those sites.

“HIV prevention efforts also should be gender-specific, targeting the important differences we have found in sexual and drug-use behaviors among men and women that increase their risk of acquiring and transmitting HIV,” Dr. Strathdee says. “For example, women IDUs in stable relationships could be shown how to negotiate condom use with their partners and offered couple counseling to educate both partners about HIV risks associated with their drug use and sexual behaviors. We need more research to identify and evaluate HIV prevention approaches for male IDUs who have sex with men to determine what kinds of interventions might work.”

Source

- Strathdee, S.A., et al. Sex differences in risk factors for HIV seroconversion among injection drug users. *Archives of Internal Medicine* 161:1281–1288, 2001.



NIDA Announces Science-Based Principles of HIV Prevention in Drug Users

During the past 15 years, NIDA research on the co-occurring epidemics of drug abuse and HIV/AIDS has yielded a set of prevention principles to guide community planners, policymakers, service providers, and medical practitioners. To foster widespread application of these science-based principles in programs to prevent the spread of HIV and other infections among drug users and their sexual partners, NIDA has prepared a new handbook: *Principles of HIV Prevention in Drug-Using Populations*.

NIDA research on the co-occurring epidemics of drug abuse and HIV/AIDS has yielded a set of prevention principles to guide community planners, policymakers, service providers, and medical practitioners.

Scheduled for release in summer 2002, the handbook summarizes the overarching principles that characterize effective HIV/AIDS prevention in drug-using populations, elaborates on these principles in a “frequently asked questions” section, describes the epidemiology of HIV/AIDS risk behaviors, and provides an overview of related, NIDA-supported research programs. The 17 science-based prevention principles are:

- Reducing the risk of HIV/AIDS in drug users is an achievable goal.
- A community must start HIV/AIDS prevention programs as soon as possible.
- Effective prevention programs require a comprehensive range of coordinated services.
- Prevention programs should work with the community to plan and implement interventions and services.
- Prevention programs must be based on a thorough, continuing assessment of local community needs, and the effectiveness and impact of these programs must be continually assessed.
- Prevention services can most effectively reach drug-using populations when they are available in a variety of locations and at a range of operating times.

- Prevention and treatment efforts should target drug users who already have HIV infection, as well as their sex partners.



HIV prevention interventions must be personalized for each individual at risk.

- Prevention efforts must target not only individuals, but also couples, social networks, and the broader community of drug users and their sex partners.
- Community-based outreach is an essential component of HIV/AIDS prevention and must be directed to drug users in their own neighborhoods.
- Prevention interventions must be personalized for each person at risk.
- Drug users and their sex partners must be treated with dignity and respect and with sensitivity to cultural, racial/ethnic, age, and gender-based characteristics.
- As part of a comprehensive HIV prevention program, injection drug users should have ready access to sterile injection equipment to reduce their use of previously used injection equipment.
- In a comprehensive program, interventions that target injection risk must address sharing other injection equipment in addition to syringes.
- While necessary, risk-reduction information alone cannot help drug users and their sex partners make lasting behavioral changes.
- Prevention efforts must address the risks of transmitting HIV and other infections sexually as well as through drug injection.
- HIV/AIDS risk-reduction interventions must be sustained over time.
- Community-based prevention is cost-effective. **NN**

NIDA Research Advances Global Efforts To Prevent and Treat AIDS

By NIDA Acting Director Glen R. Hanson, Ph.D., D.D.S.

In the 20 years since AIDS was first identified, the disease has killed 25 million people. From the beginning of the epidemic, drug abuse has played an important role in transmitting HIV, the virus that causes AIDS. Injection drug use has accounted for approximately 35 percent of the 774,467 AIDS cases reported in the United States through 2000 and is now the predominant mode of HIV transmission in many areas of the world.

Injecting drug users (IDUs) can acquire and transmit HIV when they share syringes and other paraphernalia for preparing and injecting drugs. Injecting and non-injecting drug users also are at increased risk for engaging in unprotected sexual activity, which, in turn, can result in acquisition or transmission of HIV. Finally, women who abuse drugs or have sexual contact with drug abusers have elevated rates of HIV and so are more likely than women who don't engage in these behaviors to give birth to HIV-infected infants.

NIDA-supported research on drug abuse has greatly increased our understanding of the complex role drug abuse plays in the HIV/AIDS epidemic, fueled the development of a broad range of HIV prevention and treatment approaches for drug abusers and their sexual partners, and helped reduce the spread of HIV/AIDS in the United States. In the past few years NIDA also increased its response to the global spread of HIV by expanding its efforts to foster international research and exchange scientific findings on drug abuse-related HIV/AIDS with other nations.

Research has shown that drug abuse treatment is one of the most effective ways to curtail the spread of HIV and its health consequences. For example, one recent study found that IDUs in methadone treatment contracted HIV at one-sixth the rate of IDUs who were not in treatment.

Unfortunately, approximately 85 percent of chronic drug abusers are not in treatment, so strategies to reach this population are also extremely important. Two major NIDA-supported HIV prevention research studies have shown that comprehensive community-based outreach



Research has shown that drug abuse treatment is one of the most effective ways to curtail the spread of HIV and its health consequences.

programs for out-of-treatment drug abusers can be doubly beneficial in reducing HIV transmission—they recruit drug abusers into treatment programs and they help to reduce AIDS-related risk behaviors even among those who do not have access to or are not ready to begin treatment. Over 15 years, 60,000 IDUs and their sex partners in communities across the Nation participated in the research that produced these results.

To facilitate the widespread application of research-based HIV-prevention information, NIDA recently issued *The NIDA Community-Based Outreach Model: A Manual To Reduce the Risk of HIV and Other Blood-Borne Infections Among Drug Users*. Initially developed for IDUs, the model has been adapted successfully for crack cocaine users, tailored to specific at-risk groups, and found to be effective with drug-using populations regardless of race, ethnicity, gender, and HIV status. In 2002, NIDA

plans to publish another manual detailing the essential research-based principles of HIV prevention for out-of-treatment drug abusers.

NIDA-supported research also has improved our understanding of the clinical course of HIV/AIDS in drug users. For example, a study that followed more than 200 IDUs for 10 years after they became HIV-positive found that women develop AIDS as swiftly as men despite having much lower levels of the virus in their blood during the early years of HIV infection. Such findings help shape HIV treatment for drug users and inform guidelines used by clinicians to provide women with potent antiretroviral medications and other medical care to retard AIDS' deadly advance.

While progress in the fight against AIDS has been significant, the constantly evolving dynamics of the epidemic continue to pose challenges for drug abuse research. NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse, which coordinates NIDA's AIDS research, has identified several areas for increased emphasis. These include developing approaches to preventing and treating drug abuse and its medical

consequences among women, including those who are pregnant, and the prevention and treatment of other blood-borne and sexually transmitted diseases, such as hepatitis B and C, which are prevalent in drug users and their sexual partners. The same behaviors spread hepatitis and HIV among drug abusers and it is more difficult to treat patients who suffer from both diseases.

NIDA supports efforts to develop effective HIV prevention and treatment approaches with scientists and public health officials around the world.

Also receiving increased emphasis will be HIV prevention in adolescents and other populations at risk for drug abuse and for acquiring or transmitting the virus. Findings from HIV-related research will be disseminated widely for use by practitioners and the general public. For example, NIDA recently launched a series of public service announcements to increase awareness among young people that drug use can lead to risky sex that can transmit HIV/AIDS. The announcements reinforced the theme of World AIDS Day 2001: "Youth and AIDS in the 21st Century." (See "PSAs Warn Young Adults: Drug Use Can Impair Judgment, Result in Health Problems," *NIDA NOTES*, Vol. 17, No. 1.)

In contrast to the progress we have made against AIDS in the United States, the global epidemic continues to

escalate. More than 40 million people worldwide now are estimated to be living with HIV/AIDS with 5 million new infections occurring in 2001. NIDA has responded by collaborating with other NIH institutes, the World Health Organization, and other agencies to support efforts to develop effective HIV prevention and treatment approaches with scientists and public health officials around the world.

In July 2000, NIDA cosponsored a conference in Durban, South Africa, on the relationship between drug abuse, HIV/AIDS, and poverty, where researchers from both countries shared strategies for HIV prevention, treatment, and future research. In October 2001, NIDA cosponsored the fourth annual meeting of the Global Research Network (GRN) on HIV Prevention in Drug-Using Populations in Melbourne, Australia. As one of the founding organizations of the GRN, NIDA helps support its critically important efforts to exchange scientific information and develop collaborative research on international HIV trends and prevention strategies.

In the years ahead, developing and implementing effective HIV prevention and treatment for drug abusers and their sexual partners is likely to offer the greatest opportunity for making further progress against AIDS and other blood-borne infectious diseases around the world. As it has to date, NIDA's multidisciplinary AIDS research program—in partnership with other medical, governmental, and private initiatives—will continue to be a formidable force in reducing the ravages of drug abuse and HIV/AIDS. **NN**

Prevention Program for HIV-Positive Youths Reduces Risks of Further HIV Transmission

By Patrick Zickler, *NIDA NOTES* Staff Writer

Youths between the ages of 13 and 24 account for 18 percent of reported HIV cases in the United States. If these youths engage in unsafe sexual behaviors or injection drug use, they risk infecting others or becoming infected with new strains of HIV. To help reduce these risks, NIDA-supported researchers at the University of California, Los Angeles (UCLA), have developed intervention programs designed specifically to reduce unsafe behaviors by HIV-positive youths.

Dr. Mary Jane Rotheram-Borus and colleagues at UCLA's Center for HIV Identification, Prevention, and Treatment Services designed the intervention programs—"Act Safe" and "Stay Healthy"—and evaluated their impact on risk-related behaviors of 208 youths aged 13 to 24. They found that the Act Safe program reduced both substance abuse and high-risk sexual behaviors that contribute to the spread of HIV and that participants in the Stay Healthy program were more likely than nonparticipants to make lifestyle changes that improved their own health. "It is important to change risk behaviors in infected youth both for their self-protection and to prevent transmission to others," Dr. Rotheram-Borus says.

The participants were recruited from HIV/AIDS care programs for adolescents in Los Angeles, Miami, New York City, and San Francisco and had tested positive for HIV 2 years, on average, before being enrolled. Most (78 percent) were male, 88 percent of whom were homosexual. Roughly 15 percent of participants reported injection drug use. Sexual behaviors were the most likely route of infection for most participants, according to Dr. Rotheram-Borus.

The Stay Healthy program consisted of 12 group counseling sessions conducted over 3 months. In the sessions, 12 to 15 participants and 2 counselors focused on coping with HIV status, developing healthier daily routines, and participating in health care decisions. Six months after the



HIV-positive youths who attended intervention sessions designed to reduce unsafe behaviors were more likely than nonparticipants to make lifestyle changes that improved their own health and less likely than nonparticipants to engage in sexual behaviors that might infect others.

sessions ended, participants had adopted more positive lifestyle changes than those who had not attended the intervention programs. These changes included improved diet, exercise, and sleep patterns as well as improved living arrangements and more frequent visits to health care facilities. Participants also showed improvement in a summary assessment of 23 physical health measures. Overall, females improved more than males.

The Act Safe program consisted of 11 small-group sessions conducted over 3 months.

Participants were counseled in ways to identify and change substance abuse and sexual behaviors that increased their risk of transmitting HIV or of contracting additional infections. The researchers conducted followup assessments 6 months after the sessions ended. Compared with their behavior before participation, those who attended the Act Safe sessions reported having 45 percent fewer sex partners; 50 percent fewer of the sex partners were HIV-negative or had unknown HIV status. Compared with youths who did not participate in the interventions, attendees were more likely to use protection during sex. Protected sex was less common—for attendees and nonattendees—with partners known to be HIV-positive than with partners of negative or unknown HIV status, Dr. Rotheram-Borus says. Use of drugs and alcohol dropped by nearly a third (31 percent) among those who attended the Act Safe sessions.

"These results are generally very encouraging," Dr. Rotheram-Borus says. "Risk behaviors went down, healthy behaviors went up, and the effect seems to be persistent; the gains from the interventions were maintained at least through 6 months after the sessions ended."

The youths enjoyed the small-group format, but scheduling problems and fear of stigmatization reduced attendance, Dr. Rotheram-Borus says. Only about half (51 percent) of the participants attended 6 or more of the 12 Stay Healthy sessions, and 53 percent attended 5 or more of the 11 Act Safe sessions.

“These interventions work. The next step is to develop alternative ways to deliver the same product that better accommodate the youth we are trying to reach,” Dr.

Rotheram-Borus says. “We are now developing group sessions that can be conducted by telephone and evaluating efficient ways to provide individual sessions.”

Source

- Rotheram-Borus, M.J., et al. Efficacy of a preventive intervention for youths living with HIV. *American Journal of Public Health* 91(3):400–405, 2001. **NN**

PSAs Warn Young Adults: Drug Use Can Impair Judgment, Result in Health Problems

“Jack and Jill went up the hill . . .,” but what happens next is not your typical nursery rhyme.

Using up-to-the-minute slang and animation, NIDA’s new series of TV public service announcements (PSAs) is designed to engage young viewers with a cautionary tale about the dangerous link between drug use and sexual transmission of HIV/AIDS. Among 13- to 24-year-olds with diagnosed HIV infection in 1999, nearly half of the cases (49 percent) were attributed to sexual transmission.

The messages show that when people take drugs, their judgment suffers, and they may fail to consider the possible health consequences of sexual activity. The conclusion is, “When you use drugs, there’s no happy ending. Keep your body healthy. Don’t use drugs.”

Broadcast outlets received eight versions of the 30-second PSA. Six are in English, three narrated by a male and three by a female, each narrator addressing general drug use, ecstasy use, and World AIDS Day. In the two Spanish versions of the PSA, titled “Juan y María,” a male announcer presents the general drug use and World AIDS Day messages.

Radio versions of the PSAs were released in January, and NIDA is also distributing print ads from the Jack and Jill campaign for national publication in such markets as TV magazines included in Sunday newspapers. Marvel Comics included a full-page Jack and Jill ad in one of its December 2001 editions. **NN**



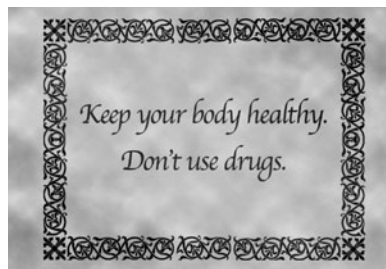
Announcer: *The National Institute on Drug Abuse presents a tale about the dangers of drugs entitled “Jack and Jill.”*



Jill got dizzy and so did he. They both got busy and felt so free.



Never did it occur that the other may be, the one infected with HIV.



Announcer: *When you use drugs, there’s no happy ending. Keep your body healthy. Don’t use drugs.*

Preventing Drug Abuse-Related Infectious Diseases Through Community Outreach

Drug abuse service providers in the field now have a new tool to help them reduce the spread of drug-related disease among drug abusers. *The NIDA Community-Based Outreach Model: A Manual To Reduce the Risk of HIV and Other Blood-Borne Infections Among Drug Users* is designed to help community planners, policymakers, program developers, and service providers develop outreach programs to prevent the spread of infectious diseases associated with drug use—primarily HIV/AIDS, hepatitis B (HBV), and hepatitis C (HCV).

The manual is based on more than 15 years of NIDA-supported research in nationwide HIV prevention projects. The Outreach Model, tested in 52 U.S. communities with more than 60,000 injection drug users, 14,000 crack users, and many of their sexual partners, has been found effective with drug-using populations regardless of race, ethnicity, gender, and HIV status.

In more than 30 studies using community-based outreach, a significant proportion of participating drug users:

- entered drug treatment;
- stopped or reduced their frequency of injection; reuse of needles, syringes, other injection equipment; and use of crack cocaine;
- increased condom use and reduced the frequency of unprotected sex;
- obtained HIV testing with counseling before and after the tests; and
- averted HIV infection.

Published last fall, the manual guides outreach workers step by step on how to select outreach sites where drugs are purchased and used, engage drug users, and educate

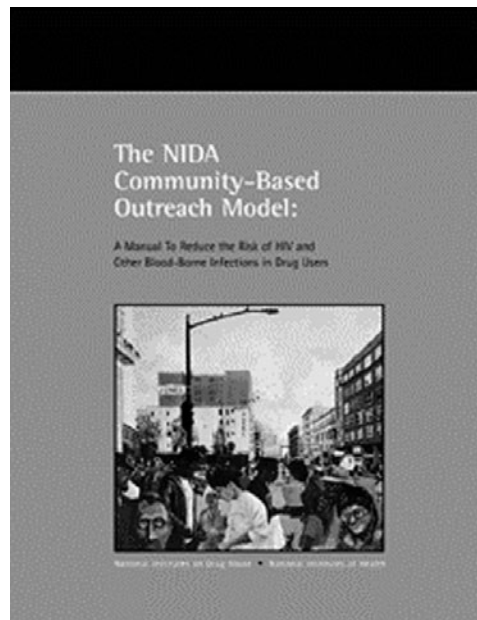
and counsel drug users about reducing their drug- and sex-related risks for infection. The community-based approach typically relies on outreach workers who are indigenous to the community and thus uniquely able to serve as role models, educators, and advocates for drug users.

The outreach manual helps community workers choose an appropriate “base” site, such as a converted recreational vehicle or mobile home; contact drug users where they congregate; open conversations with individuals at risk for infection; and enlist those individuals to attend counseling and education sessions in connection with HIV testing. Additional program services are recommended, such as couples or group counseling and sexually transmitted disease screening, diagnosis, and treatment and HIV treatment. Alternatively, it is recommended that outreach workers provide referrals for those services.

The manual recommends that drug users recruited to attend the 20- to 30-minute education and counseling sessions be provided accurate and up-to-date information on risky behaviors, concrete strategies and behavioral skills for reducing drug-using and sexual risks, and reinforcement for behavior change. A set of 24 cue cards guides counselors and drug

users through the sessions, leading logically from “What is HIV/AIDS? HBV? HCV?” to how the infections are transmitted and how drug users can reduce their risk.

The education sessions give clear, detailed instructions for reducing the risks related to drug use and sexual activity, and they promote addiction treatment as the best method of disease prevention. The NIDA Community Outreach Model recommends HIV, HBV, and HCV testing, followed by appropriate counseling on positive or negative results. **NN**



Gender Differences in Drug Abuse Risks and Treatment

Over the past few years NIDA has made a major research commitment to identifying and understanding differences in the ways that women and men—or girls and boys—are first exposed to drugs, in their risks of abuse and addiction, and in the effectiveness of drug treatment. Understanding these differences, and incorporating that understanding into drug abuse prevention and treatment, can reduce the dangers and improve outcomes. NIDA-supported research has shown that gender differences play a role from the very earliest opportunity to use drugs, that women and men tend to abuse different drugs, that the effects of drugs are different for women and men, and that some approaches to treatment are more successful for women than for men.

Are Women Less Likely Than Men to Abuse Drugs?

Men are more likely than women to have opportunities to use drugs, but men and women given an opportunity to use drugs for the first time are equally likely to do so and to progress from initial use to addiction. However, women and men appear to differ in their vulnerability to some drugs. Both are equally likely to become addicted to or dependent on cocaine, heroin, hallucinogens, tobacco, and inhalants. Women are more likely than men to become addicted to or dependent on sedatives and drugs designed to treat anxiety or sleeplessness, and less likely than men to abuse alcohol and marijuana. There are also differences between men and women who seek treatment for drug abuse. Women in treatment programs are less likely than men to have graduated from high school and to be employed and are more likely than men to have other health problems, to have sought previous drug treatment, to have attempted suicide, and to have suffered sexual abuse or other physical abuse.

Are There Gender Differences In the Biological Effects of Drugs?

Animal research and human studies have revealed that males and females may differ in their biological responses to drugs. In studies of animals given the opportunity to self-administer intravenous doses of cocaine or heroin, females began self-administration sooner than males and administered larger amounts of the drugs. Women may be more sensitive than men to the cardiovascular effects of cocaine. In human studies, women and men given equal doses of cocaine experienced the same cardiovascular response despite the fact that blood concentrations of cocaine did not rise as high in women as in men. In

studies involving long-term cocaine users, women and men showed similar impairment in tests of concentration, memory, and academic achievement following sustained abstinence, even though women in the study had substantially greater exposure to cocaine. Women cocaine users also were less likely than men to exhibit abnormalities of blood flow in the brain's frontal lobes. These findings suggest a sex-related mechanism that may protect women from some of the damage cocaine inflicts on the brain.


Does Gender Play a Role in Nicotine Addiction?

Women and men are equally likely to become addicted to nicotine, yet women typically smoke cigarettes with lower nicotine content than those smoked by men, smoke fewer cigarettes per day, and inhale less deeply than men. Overall, however, women are less successful than men in quitting smoking and have higher relapse rates after they do quit. Treatment involving nicotine replacement therapy—nicotine gum or patch—works better for men than for women.

What Are Women's Risks for HIV/AIDS?

Research suggests that there are sex-related differences in some fundamental aspects of the HIV/AIDS disease process. For example, an HIV-infected woman with half the amount of virus circulating in the bloodstream as an infected man will progress to a diagnosis of AIDS in about the same time. And, according to the Centers for Disease Control and Prevention, among cases that progress to a diagnosis of AIDS, drug abuse accounts for a greater percentage of cases among women than among men. Nearly half (47 percent) of all women diagnosed with AIDS are injecting drug users (IDUs), whereas among men, IDUs account for 32 percent of AIDS cases. An additional 19 percent of women, compared with 2 percent of men, with AIDS report having sex with users who inject drugs. In all, drug abuse is nearly twice as likely to be directly or indirectly associated with AIDS in women (66 percent) as in men (34 percent).

For More Information

NIDA's gender-related research is discussed in *Drug Addiction Research and the Health of Women*, available on NIDA's home page on the World Wide Web: www.drugabuse.gov. 

Heating Solutions Used in Drug Injection May Inactivate HIV

A NIDA-funded study has found that heating drug solutions containing HIV to 65 degrees centigrade (149 degrees Fahrenheit) may inactivate the virus. Heating drug solutions for at least 15 seconds can achieve this temperature and may reduce the potential for HIV transmission among injecting drug users (IDUs) who share the solution, the study indicates.

The study, led by Dr. Michael Clatts of National Development and Research Institutes in New York City, first observed injection equipment and practices used by out-of-treatment IDUs in New York City and Denver when they prepared drug solutions for shared injection. Laboratory studies conducted by Dr. Robert Heimer

of Yale University School of Medicine in New Haven, Connecticut, then found that HIV in cookers—typically spoons or bottle caps in which drugs are mixed with water and heated before injection—was inactivated once the temperature reached 65 degrees centigrade. Thin bottle-cap cookers reached this temperature fastest, the researchers say.

These findings indicate that HIV prevention strategies should convey the message to IDUs that heating drug solutions for at least 15 seconds can reduce the spread of HIV, the researchers conclude. The study appeared in the *Journal of Acquired Immune Deficiency Syndrome*. **NN**

Drug Abuse Treatment Programs Make Gains in Methadone Treatment and HIV Prevention

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug abuse treatment programs have substantially improved their methadone treatment practices and increased their HIV prevention efforts since the late 1980s, according to recent NIDA-funded research. These improvements appear to be partly the result of NIDA's efforts to improve drug abuse treatment and HIV/AIDS outreach.

Clinical studies conducted in the late 1980s and early 1990s indicated that methadone treatment is more likely to reduce heroin use if the dose level is at least 60 milligrams per day (mg/day), if patients are given a voice in determining their dose levels, and if no restriction is placed on treatment duration. Subsequent research, however, indicated that the majority of the Nation's methadone treatment facilities were dispensing methadone doses less than 60 mg/day, were not giving patients a voice in dosage decisions, and were encouraging patients to stop taking methadone in 6 months or less.

In response to this situation, NIDA and other Federal agencies took steps to improve methadone treatment. NIDA funded an Institute of Medicine report that recommended changes in heroin addiction treatment practices and their regulation. NIDA also funded the development of a quality assurance program that evaluates methadone treatment facilities in terms of patient outcomes. In addition, the Center for Substance Abuse Treatment (CSAT) developed a set of methadone treatment guidelines and distributed them to State substance abuse agencies and treatment providers around the country.

To determine whether these efforts were in fact improving methadone treatment practices, in 1995 Dr. Thomas D'Aunno of the University of Chicago and his colleagues at the University of Michigan in Ann Arbor collected data from 116 methadone treatment facilities located throughout the country and compared them with data collected on these same facilities in 1988 and 1990. Results showed improvement during the 7-year period, particularly regarding methadone dosage. The average dose was 45 mg/day in 1988 and 46 mg/day in 1990. By 1995, however, the average dose had increased to 59 mg/day. Also, more programs were allowing patients to participate in dosage decisions, and more programs were waiting at least a year before encouraging patients to stop taking methadone.

"Although these results show that methadone treatment facilities have made substantial improvements, we still need to make more progress," says Dr. D'Aunno. "We found an average dose of 59 mg/day in our sample of treatment facilities, but recent research indicates that doses between 80 and 100 mg/day may be the most effective in reducing heroin use."

The study found differences in treatment practices in different areas of the country and for different population groups. Dr. D'Aunno suggests that efforts targeted at particular groups of programs may be a further step to improve treatment.

The treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios.

Dr. Bennett Fletcher of NIDA's Division of Epidemiology, Services, and Prevention Research agrees that efforts to improve methadone treatment practices should continue, but adds that misunderstandings some patients have about methadone may also contribute to the problem. For example, he says, some patients attribute adverse effects to methadone that it actually does not cause. "These patients may develop medical or dental problems while taking heroin, but they don't notice them either because of heroin's analgesic effect or because they are distracted by withdrawal symptoms during abstinence," he says. "Once they're in methadone treatment and physiologically stabilized, the medical or dental problems are unmasked. It is easy to blame methadone for these problems, when in fact they were pre-existing." These misunderstandings may cause some patients to request lower methadone doses or to stop methadone prematurely, says Dr. Fletcher.

The Bandwagon Effect

Dr. D'Aunno, along with colleagues at the University of Iowa in Iowa City and the Centers for Disease Control and Prevention in Atlanta, also evaluated treatment facilities' HIV prevention efforts, including HIV testing, counseling, and outreach. For this project, they used data collected from the sample of methadone treatment facilities plus other substance abuse treatment facilities for a total of 618 facilities.

As with the methadone treatment practices, the investigators found that the facilities had made substantial improvements in their HIV prevention efforts over the period from 1988 to 1995. In both 1988 and 1990, only 39 percent of the facilities provided HIV testing and counseling, but by 1995, 61 percent were providing these services. Also, 51 percent of the facilities in 1988 and 65 percent in 1990 were engaging in HIV outreach, but by 1995 this had increased to 75 percent.

The investigators found that the treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios. Also, these facilities generally were publicly rather than privately funded and had clinical supervisors who supported HIV prevention practices.

Perhaps the most important factor in promoting HIV prevention practices, however, seemed to be pressure from people in the drug abuse treatment field. "When the HIV epidemic first started, many treatment facilities were uncertain how to react," says Dr. D'Aunno. "As some facilities began conducting HIV testing, counseling, and outreach, pressure began to mount for other facilities to do the same. This eventually created a bandwagon effect."

NIDA helped get the bandwagon going by supporting research programs in which scientists worked together with practitioners to develop effective HIV/AIDS outreach techniques, according to Dr. D'Aunno. "These programs set a good example for treatment providers," he says. "The providers saw local researchers and other providers working together on HIV prevention, and they decided to follow their lead."

Sources

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Addressing the Medical Consequences of Drug Abuse

By NIDA Director Alan I. Leshner, Ph.D.

When people hear the words “consequences of drug abuse,” they usually think of addiction, crime, and other social disruptions. However, the most immediate, extensive, and long-lasting problems caused by drug abuse, both for individuals and for society, are often medical in nature. For example, known drug abuse-related health problems and resulting lost productivity alone cost our society more than \$33 billion each year.

Illicit drugs directly cause many medical problems. Stimulants such as cocaine and methamphetamine increase the heart rate while constricting the blood vessels; in susceptible individuals, these two actions together set the stage for cardiac arrhythmias and strokes. The club drug methylenedioxymethamphetamine (MDMA, also called “ecstasy”), which many users mistakenly believe to be safe, has caused malignant hyperthermia, permanent kidney damage, and death. MDMA also damages serotonin nerve fibers in the brain. Heroin can cause a life-threatening kidney condition called focal glomerulosclerosis. The list continues: NIDA research has shown that almost every drug of abuse harms some tissue or organ.

The circumstances and behaviors associated with drug abuse add to the adverse impacts on health. Inadequate housing and poor nutrition, common accompaniments of drug abuse, can increase exposure to diseases and reduce ability to fight off infections. Injecting drug use promotes blood clots, severe skin infections, and blood-borne infections including life-threatening endocarditis, viral hepatitis, and HIV/AIDS. Abuse of some drugs is associated with impulsive sexual activity that elevates individuals’ risks for acquiring and transmitting HIV/AIDS and other sexually transmitted diseases.

The hepatitis C virus (HCV) is another blood-borne pathogen that is easily transmitted through contaminated drug injection paraphernalia. In some NIDA-funded studies nearly two-thirds of individuals have acquired HCV within 1 year of beginning injection drug use. Screening studies have found that 70 to 90 percent of individuals in some drug-injecting populations are infected and at risk

for developing chronic liver inflammation and hepatic cancer or liver failure requiring transplantation.

Many of the health consequences of drug abuse also have implications for the health of the non-drug-abusing public. Tuberculosis (TB) is an important example. Chronic drug abusers have higher rates of TB infection and disease than the general public, largely because inadequate nutrition, HIV/AIDS, and other factors lower their resistance. Reducing this high prevalence by screening and treating infected drug abusers is an important strategy in efforts to control TB in the Nation.



NIDA research has shown that almost every drug of abuse harms some tissue or organ.

NIDA-sponsored research, much of it carried out under the auspices of the Institute’s Center on AIDS and Other Medical Consequences of Drug Abuse, has made crucial contributions to understanding drug-related behavioral risks in the spread of infectious diseases and to reducing the incidence and impact of HIV, HCV, and TB among drug abusers and other at-risk populations. For example, research has shown that, contrary to what was once assumed, individuals who

enter treatment for their drug abuse and receive appropriate management and followup can adhere to the complicated, lengthy medication regimens necessary to control these diseases. This is an extremely important finding, since finishing the entire regimen is crucial to successful treatment and also to prevent the growth of resistant viral or bacterial strains that can withstand currently available medications and potentially give rise to devastating epidemics.

NIDA-supported research has also demonstrated that drug abusers are willing and able to change their behaviors to prevent HIV transmission. For example, researchers have documented reductions in HIV risk behaviors among drug abusers who were contacted by a 21-site community-based prevention outreach program. Significant numbers of drug abusers stopped injecting or lowered their frequency of injecting, stopped reusing syringes or started disinfecting syringes, and entered treatment as a result of the outreach activities.

While we now know that chronic drug abusers can comply with medication regimens, we also know that a large percentage of them do not. Thus we still need to learn much more about both adapting medication regimens for drug abusers and techniques for increasing their adherence. Moreover, some illicit drugs and drug abuse medications can interact with medications used for treating diseases, resulting in possible loss of efficacy and adverse effects. An extremely important interaction can take place, for example, between methadone and the protease inhibiting drugs that are currently the most effective treatments for HIV infection. The result can be ineffectiveness and increased toxic side effects from one or both drugs. In some cases, the presence of a protease inhibitor has inhibited the processing of methadone sufficiently to cause patients to develop symptoms of withdrawal. The identification of such interactions and development of alternative regimens is a high NIDA priority.

As the issue of drug-and-medication interactions illustrates, the approaches to drug abuse and its medical consequences must be integrated if optimal results are to be achieved. A NIDA-supported project at Montefiore Hospital in The

Bronx, New York, has demonstrated that offering drug abuse treatment and primary care services at the same site can reduce the occurrence and severity of medical consequences of drug abuse. In what appears to be another very promising intervention, NIDA is evaluating the use of mobile health vans that reach out to drug abusers with both treatment and primary care. In 9 cities, vans are regularly visiting poor and medically underserved neighborhoods with concentrated populations of drug abusers. Each is staffed and equipped to provide drug abuse counseling and referral, vaccinations and screening for common and dangerous diseases, prevention education, and limited primary care. For patients with complicated medical conditions, the vans also provide referrals to local hospitals and clinics. During the 4 years that the mobile vans have been in service, their staff has seen drug abusers gradually develop the confidence to come forward for care, then start to bring friends and family members with them. Novel approaches such as these are only first steps toward fully integrating drug abuse and overall medical treatment for chronic drug abusers—but as always, the first steps are critical to get the momentum started. **NN**

Among Drug Users, Peers Can Help Spread the Word About AIDS Prevention

By Steven Stocker, *NIDA NOTES* Contributing Writer

In traditional AIDS prevention programs, professional outreach workers inform injecting drug users (IDUs) about drug-related and sexual behaviors that can lead to HIV infection. NIDA-supported research is demonstrating that recruiting IDUs to help disseminate this information may be a way to reach more drug users and reduce their risky behaviors.



Dr. Carl Latkin (left) and ethnographer James Peterson in the Baltimore neighborhood where they enlisted the help of injecting drug users to reduce the spread of HIV in the drug-using community.

Dr. Robert Broadhead, Dr. Douglas Heckathorn, and their colleagues at the University of Connecticut in Storrs recruited IDUs in Middletown, Connecticut, to educate their peers about reducing the spread of HIV and give them HIV prevention materials, such as condoms and bleach for cleaning their syringes. The IDU recruiters also encouraged their peers to visit a storefront office where they would be tested for HIV and learn more about how to reduce their risk of contracting AIDS.

At the storefront, program staff gave IDUs a brief AIDS prevention quiz to determine how well the IDU recruiter had educated them in the community. The staff also interviewed IDUs about their HIV risk behaviors, counseled them about how to reduce these behaviors, and tested them for HIV. Each IDU was given the opportunity to recruit and educate three peers for compensation. These

IDUs, in turn, were given the opportunity to recruit and educate still more peers. Thus the number of recruits grew rapidly.

The researchers compared the effectiveness of this approach, called peer-driven intervention, with the more common approach involving outreach workers, called traditional outreach intervention. In the traditional approach, three salaried outreach workers in Windham, Connecticut, were instructed to recruit new IDUs, educate them about AIDS prevention, and encourage them to visit a storefront in Windham. Frequently, traditional outreach workers are former drug users from the neighborhood. When the IDUs came to the storefront, they received the same intervention as the IDUs in Middletown, except that they were not given the opportunity to recruit their peers.

Over a 2-year period, the researchers found that the peer-driven intervention recruited 317 IDUs, 36 percent more than the 233 recruited in the traditional approach. The IDUs recruited by peers were more representative of the racial and ethnic composition of the community. The



Dr. Douglas Heckathorn (left), Dr. Robert Broadhead, and their colleagues found that injecting drug users (IDUs) educated about HIV risk reduction by peers shared injection paraphernalia and injected drugs less often than did IDUs educated traditionally.

peer-driven intervention was also more effective in reducing HIV risk behaviors. In initial interviews with recruits and in followup interviews 6 months later, the

researchers found that IDUs recruited by peers shared syringes and other injection paraphernalia less often and injected drugs substantially less often than did the IDUs recruited traditionally. The peer-recruited IDUs also scored higher on the AIDS prevention quiz administered when they first visited the storefront. In addition, the researchers determined that educating IDUs in the community was much less expensive in the peer-driven intervention than in the traditional outreach.

One reason the peer-driven approach was more effective was that participant IDUs were exposed more often to HIV prevention information than in the traditional approach, says Dr. Broadhead. In the peer-driven intervention, IDUs were first educated by peer recruiters on the street, then again by program staff at the storefront. This information was reinforced three more times when the recruits educated and recruited three of their peers. Finally, the IDU recruiters were exposed to the information again when they came to collect their compensation for educating and recruiting their peers. In contrast, IDUs recruited in the traditional intervention received only two exposures—once when they were recruited on the street and then again when they visited the storefront.

About 40 percent of the IDUs in the peer-driven approach became active recruiters, says Dr. Broadhead. “We stopped paying them after three recruits, but some of them continued to bring in their peers even though they knew they weren’t going to get paid for it,” he says. He also reports that some recruiter IDUs called the storefront to speak to health educators to make sure that they were passing on correct information.

Active IDUs are more effective in recruiting and educating other drug users because the latter are more likely to listen to people whom they consider to be like themselves, Dr. Broadhead says. Active drug users may view professional outreach workers with suspicion, even if the outreach workers are former drug users, he says.

Dr. Broadhead suggests that using both IDUs and traditional outreach workers works well because the IDUs are more effective at education and recruitment in the community, while traditional outreach workers are better prepared for tasks such as interviewing, case management, and referrals to community agencies.

Outreach Boosts Peer Leaders’ Self-Image

In a related study, Dr. Carl Latkin at The Johns Hopkins University in Baltimore also used current IDUs to provide AIDS prevention information to drug users in the community. In Dr. Latkin’s study, the IDUs who conducted AIDS outreach were recommended by their peers. Drug users who volunteered for the study were asked to recommend other drug users in the community who might be

effective communicators of AIDS prevention information. These peer leaders were then invited to attend 10 training sessions, for which they were compensated. After the fourth session, the leaders began their outreach activities, for which they were not compensated.

At the end of 3 months, the researchers interviewed peer leaders and IDUs who used drugs and engaged in sexual relations with one another. The HIV-related behaviors of the peer leaders and their IDU contacts were compared to the self-reported behaviors of IDUs who received standard HIV testing and counseling from outreach workers, and the behaviors of the peer leaders were compared to their own behaviors at the beginning of the study. The scientists found that both the peer leaders and their IDU contacts were more likely to clean their syringe needles with bleach before either injecting themselves or sharing the syringe with others. Also, the leaders reported significantly more use of condoms.

In the training sessions, the leaders discussed how their attitudes toward the program changed as it progressed. Initially, they viewed AIDS outreach as theoretically important but they were not enthusiastic about engaging in the program. However, once they started their outreach activities and began to receive positive feedback from the community, they developed a higher regard for the program.

“Most of these people have had very few prosocial roles in their lives,” says Dr. Latkin. “Consequently, giving them a prosocial role that people in the community respect and consider beneficial is a powerful motivator.”

Because drug users began to view the peer leaders as experts, they started asking them about matters other than HIV prevention, such as how to get treatment for AIDS or drug addiction and how to get food, shelter, and other necessities. To help the peer leaders meet these requests, Dr. Latkin and his colleagues prepared information about health and social service agencies that peer leaders could hand out.

A surprising result of the study was the increase in condom use reported by the peer leaders. Studies have consistently found that reducing risky sexual behaviors is much more difficult than reducing risky drug-taking behaviors. Peer leaders may have increased their condom use because they wanted to live up to their new status as role models, Dr. Latkin speculates. “Also, I think that talking about condoms and carrying them around may have made them more comfortable with condoms,” he says.

Complementary Approaches

Enlisting current drug users to perform AIDS outreach may be an effective way to reach some subgroups of the drug-using population not reached by traditional outreach

workers, says Dr. Richard Needle of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse. "I think that if you are conducting an AIDS outreach project, you might want a combination of outreach workers—some of whom are current users and some of whom are not," he says. He also thinks that Dr. Broadhead's and Dr. Latkin's studies should be tested in other communities to see whether their results can be replicated.

"NIDA is interested in exploring a range of outreach strategies and trying to determine the advantages and disadvantages of each of them," says Dr. Needle. "I suspect that the different approaches will prove to be complementary."

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Gender Differences in Progression to AIDS

NIDA-funded research on injecting drug users (IDUs) conducted by Dr. Homayoon Farzadegan and his colleagues at The Johns Hopkins University School of Hygiene and Public Health in Baltimore has shown that the course of HIV infection differs in women and men, so that gender-specific treatment may be needed. This study of 2,960 adult IDUs, begun in 1988 with followup in 1992 and 1997, revealed that although women progressed to AIDS as rapidly as men, they had approximately half the viral load in their bloodstreams when they developed AIDS. Initiation of AIDS treatment is based on HIV viral

load, and current treatment guidelines are derived mainly from studies with men.

The researchers speculate that physiological factors such as hormones may account, in part, for their findings. Dr. Farzadegan and the research team believe that these gender differences must be explored further, and the possibility that women are being under-treated based on current guidelines warrants considering a change in when women start therapy. The study was published in *Lancet* in 1998. **NN**

Drug Abuse Research Helps Curtail the Spread Of Deadly Infectious Diseases

By NIDA Director Alan I. Leshner, Ph.D.

Drug abuse plays a central role in the spread of infectious diseases that threaten our Nation's health. Injection drug use now accounts for about one-third of all new cases of AIDS reported in the U.S. each year, according to figures from the Centers for Disease Control and Prevention. Other statistics show that drug abuse is strongly linked to the spread of hepatitis, tuberculosis (TB), and syphilis and other sexually transmitted diseases. To address this major public health challenge, NIDA has long supported a broad program of research on drug abuse and infectious diseases. (For more information on drug abuse and infectious diseases, see "Infectious Diseases and Drug Abuse," *NIDA NOTES*, Vol. 14, No. 2.)

Over the last decade, NIDA-funded researchers have developed and evaluated a range of interventions to reduce the spread of HIV among drug abusers, their sexual partners, and their children. Drug abuse treatment and community-based outreach and education programs have consistently demonstrated that drug abusers will reduce the drug-use and sexual behaviors that put them at risk for HIV and other blood-borne infectious diseases and that these changes in behavior lead to declines in new HIV infections. For example, one study of heroin addicts conducted by NIDA-supported researchers at the University of Pennsylvania in Philadelphia found that injecting drug users (IDUs) in a methadone treatment program contracted HIV at one-sixth the rate of addicts who were not in treatment.

NIDA-supported researchers also have contributed to meeting the serious public health challenge posed by the re-emergence of TB in the last decade. HIV became prevalent among IDUs in the mid-1980s and transformed the latent TB infection that has always been widespread in this population into the contagious form of the disease. NIDA-supported epidemiologic, community, and treatment research among drug users at high risk for HIV and



Research has consistently demonstrated that drug abusers will reduce the drug-use and sexual behaviors that put them at risk for HIV and other blood-borne infectious diseases.

TB played an important role in a coordinated Federal and State initiative that led to the implementation of effective strategies to prevent and treat TB. As a result, from a peak of 26,673 cases in 1992, new TB cases fell to an all-time low of 19,851 in 1997. (For more information, see "Linking Medical Care With Drug Abuse Treatment Stems Tuberculosis Among HIV-Infected Drug Users," *NIDA NOTES*, Vol. 13, No. 3.)

NIDA's TB and HIV research has demonstrated that providing medical care to IDUs in conjunction with drug abuse treatment can curb the spread of infectious diseases. NIDA now is promoting further research to identify factors that support or hinder linkages between drug abuse treatment and primary medical care among a variety of populations, particularly women and racial and ethnic minorities.

NIDA-supported research also has developed approaches that can check the spread of infectious diseases among the approximately 85 percent of IDUs who are not in treatment. For example, one long-term study in Baltimore providing directly observed preventive therapy and a variety of health care services in one convenient setting virtually eliminated new TB cases among out-of-treatment IDUs. We now are developing additional research initiatives to add drug abuse treatment to vans that provide comprehensive medical services in neighborhoods with large populations of out-of-treatment heroin addicts. We believe these coordinated mobile clinics may lead to further reductions in drug abuse and infectious diseases in this population.

Noninjection drug use also fosters the spread of infectious diseases. For example, smokers of crack cocaine, particularly women who exchange sex for drugs, are at high risk for infection with HIV, hepatitis, TB, and sexually transmitted diseases. In addition, it appears that many heroin users who begin by snorting that drug sooner or

later progress to injection drug use with its attendant risks. Early data from a NIDA-supported study by scientists at National Development and Research Institutes, Inc., in New York City indicate that a substantial portion of heroin snorters become injectors, engage in a high level of risky drug-use and sexual behaviors, and begin to contract hepatitis C soon after they start injecting drugs. By also shedding light on the complex individual and social factors that contribute to transition from noninjection to injection drug use, this study will help us develop new approaches to forestall the progression to injection drug use and infectious disease. (See “Heroin Snorters Risk Transition to Injection Drug Use and Infectious Disease,” *NIDA NOTES*, Vol. 14, No. 2.)

While we have made much progress in preventing and treating infectious diseases among drug abusers, the continued high prevalence of diseases such as HIV/AIDS and hepatitis in this population indicates that much remains to be done. Therefore, NIDA recently established the Center on AIDS and Other Medical Consequences of Drug Abuse. Headed by Dr. Henry Francis, the Center is coordinating a multidisciplinary program of research on the full spectrum of critical health issues associated with drug abuse. Components of the program include tracking the extent and progression of infectious diseases among drug users, assessing the effect of illicit drugs on the immune system, linking drug abuse treatment and medical care, and developing new educational and behavioral strategies for drug abusers who are not in treatment. Ultimately, the program will generate new strategies for reducing the spread of infectious diseases. (For additional information, see “New NIDA Center

Will Address Health Issues Associated With Drug Abuse,” *NIDA NOTES*, Vol. 13, No. 5.)

Because drug abuse and infectious disease have implications for many areas of biomedical research, the Center also is fostering collaborative research efforts with other institutes of the National Institutes of Health (NIH), government agencies, and private sector groups. Currently, NIDA supports more than 10 interagency and interinstitute studies involving drug abuse and infectious disease. For example, the Women and Infants Transmission Study being conducted by NIDA, the National Institute of Allergy and Infectious Diseases, and the National Institute of Child Health and Human Development is investigating mother-to-infant transmission of HIV. NIDA also is participating in a new, congressionally mandated

Early data from a NIDA-supported study by scientists at National Development and Research Institutes, Inc., in New York City indicate that a substantial portion of heroin snorters become injectors, engage in a high level of risky drug-use and sexual behaviors, and begin to contract hepatitis C soon after they start injecting drugs.

NIH research initiative that is responding to the health problems associated with hepatitis C. Approximately 4 million Americans are infected with this virus, which can cause chronic liver disease that results, in many cases, in death due to cirrhosis and liver cancer. NIDA-supported research will be critical to the success of the NIH initiative because of the major role injection drug use plays in the transmission of this insidious infection.

In the years ahead, drug abuse and infectious disease will continue to pose challenges to the Nation’s health. NIDA’s broad program of research on the medical consequences of drug abuse will continue to provide the scientific knowledge needed to overcome those challenges with multifaceted public health responses. **NN**

Heroin Snorters Risk Transition To Injection Drug Use And Infectious Disease

By Robert Mathias, *NIDA NOTES* Staff Writer

Heroin users who think they can avoid the harmful consequences of drug injection by snorting or smoking the drug may be dangerously mistaken. A NIDA-funded study indicates that noninjecting heroin users (NIUs) are at considerable risk of becoming drug injectors, thereby incurring risks for HIV, hepatitis, and other serious diseases. Moreover, regardless of whether they go on to inject drugs, a significant number contract hepatitis, the study shows.

“Becoming a drug injector is not inevitable for heroin snorters who have never injected drugs, but the risk of making the transition to injection drug use is fairly substantial,” says Dr. Alan Neaigus of National Development and Research Institutes (NDRI),

Inc., in New York City. Dr.

Neaigus and his colleagues at NDRI have been examining rates of transition to injection drug use and disease incidence among 560 NIUs recruited from March 1996 through April 1998. The study group consists of heroin users who have never injected drugs and former heroin injectors who had not injected drugs for at least 6 months prior to the study. Data from followup interviews conducted with 331 study participants show that more than 15 percent transitioned to drug injection during an average period of a little more than a year. The researchers found no significant difference in the transition rate between NIUs who had never injected heroin and the 31 percent of the study group who were former injectors.

Previous studies have found higher rates of transition from noninjection to injection drug use, particularly among former injectors. However, Dr. Neaigus says a number of factors may now be slowing the rate at which heroin snorters are initiating or resuming injection of the drug. First, a dramatic increase in the purity of heroin during the 1990s has made it possible for snorters to achieve a high that is similar to what they can obtain from injection. Second, greater awareness of the risk of contracting AIDS from injecting drugs may be dissuading more users from the practice.

The NIU study supported earlier research findings that NIUs who socialize, use drugs, or have sex with IDUs

significantly increase their risk of crossing the line from snorting to injecting drugs. Preliminary analysis further suggests that being in the presence of an IDU who is injecting drugs may play an important role both in the initiation and resumption of injection drug use, Dr. Neaigus says. This finding suggests that the direct transfer of information and techniques used to inject drugs may be an important factor in the transition to injection drug use.

The level of heroin addiction is another major factor in the transition to injection. The NIU study participants’ levels of addiction ranged from snorting heroin occasionally on weekends through using several bags a day, Dr.

Neaigus says. Previous research has suggested that even with the availability of high-purity heroin, more heavily addicted heroin snorters may turn to drug injection because it remains a more effective way to take the drug. For example, in a study conducted between 1991 and 1993 by Dr. Samuel R. Friedman, also of NDRI, 30 percent of 755 IDUs

in Brooklyn, New York, reported they started to inject to get a better high.

NIUs and Infectious Disease

The health risks associated with noninjecting heroin use are substantial, both for NIUs who become IDUs and for those who don’t, the study found. All study participants received counseling about the risks of drug injection, hepatitis, and HIV. Nevertheless, almost 23 percent of the NIUs who began to inject drugs contracted hepatitis C (HCV) over the average followup period of a little over a year. HCV leads to chronic liver infection in about 80 percent of patients, most of whom eventually develop fatal liver diseases such as cirrhosis and liver cancer, says Dr. Henry Francis, who directs NIDA’s Center on AIDS and Other Medical Consequences of Drug Abuse.

Because injection drug use is the primary mode of HCV transmission, “the rapid rate of transmission of hepatitis C among NIUs who initiate or resume injecting was expected,” Dr. Neaigus says. “However, it is still alarming,” he adds. What was unexpected was that some NIUs who did not

NIUs who socialize, use drugs, or have sex with IDUs significantly increase their risk of crossing the line from snorting to injecting drugs.

begin to inject drugs—about 4 percent—also contracted HCV during the followup period. NDRI researchers now are attempting to determine how these NIUs contracted the infection, Dr. Neaigus says.

NIUs who did not transition to injection drug use were also at substantial risk of becoming infected with hepatitis B (HBV), the study shows. About 9.5 percent contracted HBV during the followup period. Though it receives less attention than HCV, HBV can develop into chronic infection and serious liver disease in up to 20 percent of cases, says NIDA's Dr. Francis.

The considerable amount of HBV found among NIUs, particularly among those who have never injected, reflects substantial sexual transmission of this disease, Dr. Neaigus says. Though the study only measured sexual activity over a 30-day period, "we found a lot of sexual risk in this group," he says. For example, about 70 percent of NIUs were sexually active during this period with two-thirds of them engaging in unprotected sex, many with partners who had HIV or were IDUs, says Dr. Neaigus.

To date, the study has not found any new cases of HIV either among NIUs who began injecting drugs or among those who did not. However, Dr. Neaigus says that the high rates of new HBV and HCV infections found among NIUs may serve as markers for sexual behaviors and drug injection practices that continue to put NIUs at risk for infection with HIV. In addition to finding extensive high-risk sexual activity among NIUs, the study found NIUs

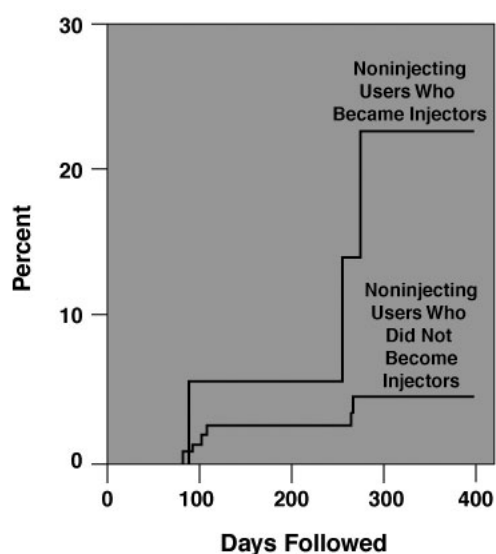
who had recently transitioned to injection drug use commonly shared injection equipment, such as cookers, cotton, and rinse water. However, they infrequently shared syringes and over half obtained all their syringes from syringe exchange programs.

Noninjection drug use is two-edged in its effect on heroin users' risk of contracting infectious diseases, Dr. Neaigus concludes. On the one hand, the considerable numbers of former IDUs who are now snorting heroin instead of injecting it have reduced their risk of AIDS and HCV considerably. On the other hand, NIUs who have never used heroin before have increased their risk of heroin addiction, transition to injection drug use, and contracting HIV, HCV, and HBV.

"This is the era of AIDS, and everyone knows about the risks from needles. When you sniff, you don't have to worry about AIDS."

— Noninjecting heroin user interviewed in New York City

Hepatitis C Among Noninjecting Heroin Users



Drug injection is the primary mode of hepatitis C transmission. In a New York City study, a large percentage of non-injecting heroin users who transitioned to injection drug use contracted the disease.

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Special Journal Supplement Summarizes Research On HIV Prevention in Drug-Using Populations

To underscore the importance of research on prevention of HIV/AIDS in drug-using populations, the publishers of Public Health Reports issued a special supplement in June 1998 focusing on the current status of national and international research on the subject. In the supplement, co-edited by Dr. Richard Needle, chief of NIDA's Community Research Branch (CRB), Dr. Susan Coyle, chief of NIDA's Clinical, Epidemiological, and Applied Sciences Review Branch, and Helen Cesari of CRB, researchers report on interventions that have proven effective in helping drug users change their behaviors and reduce their risk of HIV infection.

The supplement reviews more than a decade of HIV prevention research supported by NIDA. Research reported in the issue indicates that community-based intervention strategies have proved to be effective in averting HIV infection by providing drug-using populations with the means for changing their drug use patterns, needle practices, and sexual behaviors.

Articles highlight seven HIV prevention principles, including the need to:

- initiate HIV prevention interventions early in the epidemic;
- implement interventions at legal, institutional, community, network, and individual levels;
- implement interventions in multiple settings such as streets, shooting galleries, clinics, needle exchange programs, and drug treatment centers;
- target multiple risk behaviors such as drug use, needle risk, and sexual practices;
- provide access to risk reduction information and supplies, including injection hygiene materials, condoms, and HIV antibody testing with counseling;
- recognize that populations at risk for HIV are in varying stages of readiness to engage in interventions and create opportunities for repeated exposures; and
- be assured that risk reduction is an appropriate, realistic outcome of HIV interventions.

NIDA made this supplement available to scientists at the 12th World AIDS Conference in Geneva last summer. **NN**

Researchers Find Gender Differences In How Drug Abusers Respond To HIV Prevention Strategies

By Steven Stocker, *NIDA NOTES* Contributing Writer

Men who abuse drugs are more likely to reduce their sexual risks of HIV infection if they are given risk-reduction information on the street, while women drug abusers respond better if they are given this information in an office with counseling. This is one of the findings of a NIDA-funded study on the effectiveness of HIV risk-reduction programs tested in two towns in Arizona.

Dr. Robert Trotter and his colleagues at Northern Arizona University in Flagstaff developed two enhanced programs for reducing drug-related and sexual risks for HIV transmission and added the programs to a standard program developed by the Centers for Disease Control and Prevention and modified by NIDA. The standard program recruits drug abusers on the street and then provides HIV risk-reduction information at the project office. In the office, counselors provide information on proper condom use and bleach disinfection of drug injection equipment. Drug abusers also are offered testing for HIV infection.

One of the enhanced programs developed by the researchers, called the active outreach intervention, provides the HIV risk-reduction information on the street rather than in the office. Later, the entire network of people who use drugs together and share drug use equipment is invited into the office for a group discussion of HIV transmission risks.

The other enhanced intervention, called the office-based intervention, involves the same recruitment procedure as the standard intervention, but additional counseling techniques are used when the drug abuser visits the office. In the office, the person is first asked to identify at least one HIV risk in his or her life. The person is then asked

how this risk might be reduced and is encouraged to do so. Like the active outreach intervention, the office-based intervention also involves a subsequent group session with the network of drug abusers.



Dr. Robert Trotter of Northern Arizona University discusses with his staff possible strategies for reducing HIV transmission risks among drug abusers who use drugs together and share drug injection equipment.

All three interventions, both the standard and the two enhanced, reduced HIV risk behaviors; however, for reducing sexual risks, the researchers found that the active outreach intervention worked better for men, and the office-based intervention worked better for women. The men seemed to respond well to being taught about HIV risk-reduction on the street because that was the environment in which HIV risks often occurred, Dr. Trotter speculates. "Some pretty solid social science theory states that, for certain kinds of behavior, providing the behavior reduction intervention in the context in which the behavior occurs is more effective," he says.

However, this theory did not apply to the women in the study. The women told the researchers that they felt safe discussing sensitive matters in the office, where they were not under pressure from family and other drug abusers. "If we had conducted the interventions with these women on the street or in their homes, people would be around who might hear what they were saying, and the women were afraid of the repercussions. In the office, the women felt emotionally and physically protected," Dr. Trotter says.

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NN

Drug Abuse Cost to Society Set at \$97.7 Billion, Continuing Steady Increase Since 1975

By Neil Swan, NIDA NOTES Staff Writer

The economic cost to U.S. society of drug abuse was an estimated \$97.7 billion in 1992, according to recent calculations. The new cost estimate continues a pattern of strong and steady increase since 1975, when the first of five previous cost estimates was made. The current estimate is 50 percent higher than the most recent previous estimate—which was made for 1985—even after adjustment for population growth and inflation.

The parallel cost to society for alcohol abuse was estimated at \$148 billion, bringing the total cost for substance abuse in 1992 to \$246 billion. This total represents a cost of \$965 for every person in the United States in 1992. The per-person cost for drug abuse alone was \$383.

These estimates were calculated for NIDA and the National Institute on Alcohol Abuse and Alcoholism by The Lewin Group, a private health care research and consulting company in Fairfax, Virginia. The results were prepared by analysts using data from a variety of public and private sources and were released in May 1998 in a 220-page report, *The Economic Costs of Alcohol and Drug Abuse in the United States, 1992*.

Inflation and population growth have driven the cost of drug abuse even higher since 1992, the analysts said. Updating the estimates developed in their study, they

calculated that the cost of drug abuse increased 12.5% from 1992 to 1995, bringing the cost to \$109.8 billion in 1995.

“Substance abuse and addiction have serious medical and social consequences,” says NIDA Director Dr. Alan I. Leshner. “These rising costs warrant a strong, consistent, and continuous investment in research on prevention and treatment. We must publicize these cost-to-society estimates to educate people that drug abuse is enormously expensive to the entire Nation, that the cost has been rising steadily, that extensive research shows that drug abuse can be treated, and that drug abuse treatment reduces that cost.”

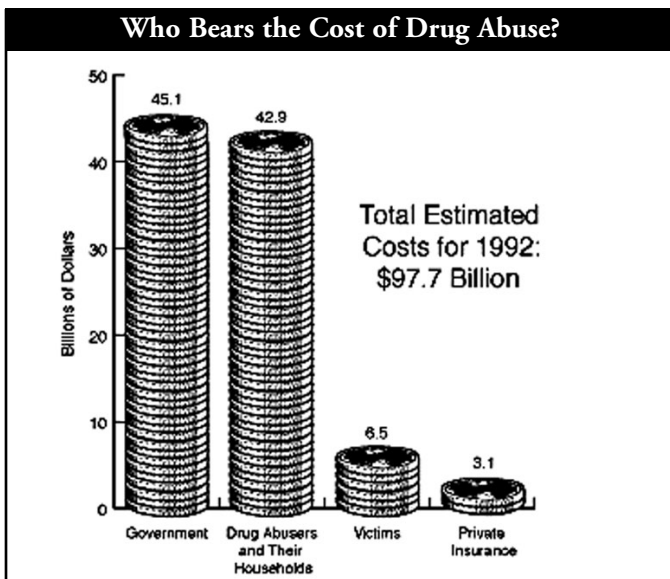
The report’s authors said substance abuse brings specific well-recognized consequences and costs in three categories: first, health consequences and their impacts on the health care system; second, criminal behavior, either as a livelihood, participation in the drug trade, or violence related to drug abuse; and finally, job losses, family impoverishment, and subsequent reliance on welfare or other elements of society’s safety net.

New Cost Estimates Reflect Recent Developments

The new cost estimates reflect major developments since the last analysis, including:

- increased availability of cocaine and crack cocaine;
- the spread of HIV and AIDS among injecting drug users;
- increasing numbers of people treated for alcohol abuse who also have drug abuse problems;
- increased availability of, and support for, substance abuse treatment, largely during the late 1980s;
- significant restructuring of the delivery of health services for drug abuse; and
- expansion of scientific knowledge about drug abuse problems and their impact on society.

The analysis notes that the epidemics of cocaine abuse and HIV/AIDS were in their early stages when the last economic cost estimate was compiled in 1985. In addition, heavy drug use was higher in 1992 than in 1985, the analysts reported.



Estimated Economic Cost of Drug Abuse In the United States, 1992 (Millions of Dollars)

Health Costs	
Direct	
Drug Abuse Services	\$4,400
Medical Consequences	\$5,531
Indirect (Lost Earnings)	
Premature Death	\$14,575
Illness	\$14,205
Institutionalization	\$1,477
Total Health Costs	\$40,188
Crime and Other Costs	
Direct	
Crime	\$17,970
Social Welfare Administration	\$337
Indirect (Lost Earnings)	
Victims of Crime	\$2,059
Incarceration	\$17,907
Crime Careers	\$19,198
Total Crime and Other Costs	\$57,471
Total Cost	\$97,659

Changes in the methodology used to calculate estimates resulted in higher cost estimates for various health problems attributable to drug abuse, the researchers say. However, while 80 percent of the increase in estimated costs of alcohol abuse can be attributed to changes in methodology in the new study, more than 80 percent of the increase in estimated costs of drug abuse is due to real changes in drug-related emergency room episodes, health service delivery trends, and criminal justice expenditures.

Law enforcement and incarceration costs played a significant role in the increases. Although crime rates remained relatively stable between 1985 and 1992, criminal justice expenditures more than doubled overall, even after adjusting for inflation. Increases in the numbers of people incarcerated were a major factor in rising drug-related costs, reflecting increases in drug-related arrests and changes in sentencing practices for drug crimes.

Health Costs

Health care expenditures for drug abuse problems were estimated to total \$9.9 billion. Of this total, \$4.4 billion was for drug abuse treatment, detoxification, and rehabili-

tation services, as well as prevention, training, and research. Treatment for drug abuse-related health problems—including HIV infection and AIDS, other diseases, and injuries—totaled \$5.5 billion. Compared to past analyses, the new estimate shows greater recognition for health-related costs of coexisting substance abuse and other medical or mental disorders.

Some 25,000 premature deaths were attributed to drug abuse in 1992, for a total cost of \$14.6 billion, a figure that represents the value of expected lifetime earnings that were lost. The analysts calculated the average loss per death at about \$350,000. Many of the deaths were among drug abusers 20 to 40 years of age, many of whom died of accidents, trauma, or HIV/AIDS.

An additional \$14.2 billion in lost potential productivity was estimated for drug-related illness and disability for 1992. This loss was in the form of work not performed, including household tasks. The authors point out that the study does not attempt to estimate the burden of drug abuse on work sites or employers because no reliable data are available on which to base an estimate.

Crime and Welfare Administration Costs

The costs of crime that were attributed to drug abuse were estimated at \$58.7 billion in 1992. Drug abuse was implicated in the cost analysis as the cause of 25 to 30 percent of all income-generating crime, such as burglary and robbery; 5 percent or less was attributed to alcohol problems. In contrast, alcohol abuse was implicated in 25 to 30 percent of violent crimes, with only 5 percent or less of violent crimes attributed to drug abuse. Criminal justice system costs due to drug abuse, including drug traffic control expenditures, totaled \$17.4 billion.

The indirect costs of drug-related crime include lost lifetime earnings of homicide victims, totaling \$1.4 billion, and \$2.06 billion in lost earnings for victims of nonfatal crimes.

Enormous costs to society were attributed to lost income for incarcerated drug criminals and lost legitimate income when individuals instead pursue illegitimate, drug-related livelihoods. Some 460,000 drug offenders were incarcerated throughout 1992, for a calculated loss of potential productivity of \$17.9 billion. What the analysts call the costs of “crime careers” were set at \$19.2 billion in 1992. This figure assumes the equivalent of 600,000 drug abusers and drug traffickers dropping out of full-time, legitimate jobs to earn their living from predatory or consensual crime, such as drug trafficking and prostitution.

Social welfare spending attributable to drug abuse-related impairments was \$3.8 billion in 1992. Of that figure, administrative costs account for an estimated \$337 million. Only these administrative costs are included in the

report's cost estimates because cash transfer programs, such as social welfare, simply represent a redistribution of resources.

Who Pays These Costs?

The Nation as a whole pays the costs of drug and alcohol abuse, the authors concluded. Many of the costs fall on the alcohol or drug abuser. Drug abusers and their families bear \$42.9 billion of the total, including costs related to health problems, early death, or lost earnings. The gov-

ernment bears the largest share, paid for services such as criminal justice. Other costs are transferred through insurance mechanisms, including welfare, health coverage, and unemployment and disability insurance.

For More Information

The Economic Costs of Alcohol and Drug Abuse in the United States, 1992 (#BKD265) is available on NIDA's Web site at www.nida.nih.gov/EconomicCosts/Intro.html.



Curbing Tuberculosis in Out-of-Treatment Injecting Drug Users

By Robert Mathias, *NIDA NOTES* Staff Writer

In addition to developing strategies to deal successfully with tuberculosis (TB) among injecting drug users with HIV in drug abuse treatment programs, NIDA-supported researchers also have developed effective approaches to preventing and treating tuberculosis among out-of-treatment injecting drug users with HIV.

Out-of-treatment injecting drug users represent an even bigger threat than those in treatment for spreading infectious diseases such as HIV and TB, says Dr. David Vlahov of The Johns Hopkins University in Baltimore. "At any one time only 15 percent of drug users are in drug abuse treatment," Dr. Vlahov says. "The question is, what do you do about the other 85 percent?" he asks. Historically, most of these individuals have had little or no access to health services where treatment for infectious diseases could be provided, he points out.

Some solutions to this problem have come from a NIDA-supported study led by Dr. Vlahov that has been following 3,000 out-of-treatment drug users in Baltimore since 1988. Dubbed the AIDS Linked to the Intravenous Experiences (ALIVE) cohort, the study was originally funded by NIDA to track how HIV/AIDS progresses in this population. Slightly more than 700 of the nearly 3,000 study participants tested positive for HIV when they were first assessed. In the succeeding 10 years, another 290 participants became HIV positive.

NIDA-supported research has shown that HIV infection can activate latent TB infection, which is widespread among injecting drug users. Thus, in 1990, the ALIVE study began to conduct TB testing on 600 HIV-positive and 600 HIV-negative study participants when they visited a community-based clinic for assessment and health care every 6 months. In 1991, the study began to offer directly observed tuberculosis prevention treatment to participants with and without HIV infection who tested positive on a skin test for tuberculosis infection. With directly observed prophylaxis, study staff observed patients take twice weekly doses of isoniazid, a tuberculosis prevention medication, for at least 6 months.

Out-of-treatment drug users do not have the incentive of getting a daily methadone dose that can bring in-treatment patients back to a clinic for regular medical treatment, Dr. Vlahov points out. Initially, the ALIVE study used street outreach, word of mouth, and a small cash payment to recruit participants for initial assessment and testing, he says. To get these participants to come back for followup assessments and treatment, the ALIVE staff provided a supportive clinic environment that offered strict confidentiality, a refuge from the street, and easily accessible health care services, he says.

"The key to providing health care services for out-of-treatment drug users is one-stop shopping combining as many services as possible in one location," Dr. Vlahov says. The clinic for ALIVE participants was located in the Baltimore City Department of Health building. A health department nurse assigned to the clinic provided TB prevention medications onsite; and patients could easily be referred to other clinics in the building for specialized health services, he notes.

As a result of offering directly observed TB therapy within this comprehensive, supportive health-care environment, "the incidence of new cases of tuberculosis among the patients in the study, which had peaked at 12 cases of active disease in 1991 when we started offering TB prophylaxis, went down to nearly zero," Dr. Vlahov says. "Basically, we've eradicated TB from our cohort," he says.

Source

- Graham, N.M.H.; Galai, N.; Nelson, K.E.; Astemborski, J.; Bonds, M.; Rizzo, R.T.; Sheeley, L.; and Vlahov, D. Effect of isoniazid chemoprophylaxis on HIV-related mycobacterial disease. *Archives of Internal Medicine* 156:889-894, 1996. **NN**

Linking Medical Care With Drug Abuse Treatment Stems Tuberculosis Among HIV-Infected Drug Users

By Robert Mathias, *NIDA NOTES* Staff Writer

Injecting drug users with HIV/AIDS can be treated successfully for tuberculosis (TB) in methadone treatment programs that provide comprehensive medical care, according to NIDA-supported research. Integrating medical care and drug abuse treatment also has been effective in preventing new cases of TB from developing among HIV-positive patients, the research indicates.

"A key to dealing successfully with infectious diseases, such as TB and HIV, among drug abuse patients is the linkage of primary care and drug abuse treatment in a drug abuse treatment setting," says Dr. Paul A. Coulis of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse. "In places where this has been done, such as New York City, it has been effective, so we know it works," he says.

TB is a chronic and infectious lung disease. People with latent tuberculosis infection do not have symptoms, may not develop active disease, and cannot spread TB. However, if such individuals do not receive preventive therapy, they may develop active TB, which is contagious.

Research has shown that injecting drug users have high rates of latent tuberculosis infection. NIDA-supported studies among injecting drug users have shown that HIV can activate this latent TB infection and increase the risk that active TB will develop. In New York City, which was hard hit by the linked epidemics of HIV and TB during the mid-1980s and early 1990s, 30 percent of persons with active TB were injecting drug users, according to the Centers for Disease Control and Prevention (CDC).

Rates of TB have declined both nationally and in New York City since 1992. However, injecting drug users continue to be at high risk for HIV and tuberculosis. For example, about one-third of the 900 methadone treatment patients in the Montefiore Medical Center's Substance Abuse Treatment Program in The Bronx, New York, have HIV, and TB rates are much higher than they are in the general population, says Dr. Marc Gourevitch, who directs a NIDA-funded study of TB infection in drug users enrolled in the program. "Almost all the active TB cases we see among drug users in our program are among those who are HIV-positive," Dr. Gourevitch notes.

To respond to the complex health needs of its patients, the Montefiore treatment program used funding from NIDA and the Health Resources and Services Administration to begin providing medical care on site along with methadone treatment in 1989. In addition to general and HIV-related

primary care, on-site services now include mental health and social support services; HIV testing and counseling; and TB testing, prevention, and treatment. "Our model has been to build comprehensive primary care services into the same site at which people are receiving their drug treatment to make it easier for them to get their medical care," Dr. Gourevitch says. This treatment model has enabled the program to achieve excellent success in getting drug abuse treatment patients to complete the full course of TB therapy needed to curtail the spread of the disease, he says.

Patients must follow demanding medication regimens to prevent and treat TB. To complete the full course of TB prevention, injecting drug users with latent TB infection must take one medication, isoniazid, daily for up to a year. Patients with active tuberculosis require an initial hospitalization with a 4-medication regimen and then must take 2 to 4 medications daily or several times a week for up to a year. Failure to complete the full course of TB treatment can spawn an even more deadly form of the disease, one that is resistant to tuberculosis medications.

In 1989, the Montefiore treatment program implemented a strategy called directly observed therapy (DOT) that was designed to increase patients' adherence to TB therapy. With DOT, treatment personnel observe patients taking each dose of their TB prevention and treatment medications. Now a widely accepted TB treatment practice, DOT, along with improved management of TB cases to ensure completion of a full course of therapy, has been credited by the CDC as playing a major role in the overall reduction in TB rates in the United States since 1992 (see "The Rise and Fall of TB in the United States."). Methadone treatment programs offer an ideal setting to implement DOT and ensure that injecting drug users complete the full course of treatment because patients are coming in daily for their methadone anyway, Dr. Gourevitch says. "It's a natural process to administer the anti-TB medications and methadone at the same time under direct supervision," he says.

Directly observed tuberculosis prevention and treatment are voluntary at Montefiore. No incentives are offered for participating in supervised preventive therapy, and methadone is not withheld if drug abuse treatment patients do not accept TB therapy. "Yet, almost everyone opts for observed therapy because it eliminates the hassle of having to remember to take TB medications at other times of the day," Dr. Gourevitch says.

Research conducted by Dr. Gourevitch shows that a high percentage of patients receiving directly observed prophylaxis and treatment in the context of their methadone treatment adhere to and complete TB therapy. In one study, more than 80 percent of 114 eligible patients had completed or were still receiving prophylaxis or treatment at the end of a 2-year period. Additional research by Dr. Gourevitch indicates that completion of TB prophylaxis was associated with a 75 percent reduction in the TB rate in this high-risk population and that providing on-site directly observed prophylaxis is cost-effective in terms of preventing the costs of treating active TB.

“What we’ve learned is that having primary care integrated with drug abuse treatment is a very effective way to treat and prevent various diseases among drug users,” concludes NIDA’s Dr. Coulis.

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The Rise and Fall of TB In the United States

After decades of decline, tuberculosis (TB) re-emerged during the 1980s to mount a new threat to the Nation’s public health. From a low of 22,201 cases in 1985, TB rates started to increase in the remaining years of the decade, according to the Centers for Disease Control and Prevention (CDC). The rise in new TB cases accelerated into the early 1990s, peaking at 26,673 in 1992.

Injecting drug use and the onset of the HIV/AIDS epidemic during the 1980s both have played important roles in the resurgence of TB. Rates of latent, or inactive, TB have always been high among injecting drug users. NIDA-supported studies show that HIV infection, which is also prevalent among injecting drug users, can activate this latent TB and accelerate the course of the disease. Lack of access to TB therapy or failure to complete a full course of therapy also contributes to development of active TB and transmission of the infection.

To counter the threat of TB, a number of Federal agencies, including the National Institutes of Health (NIH) and CDC, worked with State health departments in the early 1990s to develop a national TB elimination strategy. As a result, State and local health departments received increased Federal resources to improve their TB prevention and control programs, and NIH institutes increased their funding for TB research. The resulting NIDA-supported TB research focused on charting the course of TB among drug users and improving strategies to halt its spread by increasing drug users’ adherence to TB medication regimens.

This coordinated effort led to the development of effective strategies to identify and treat persons with TB. As a result, the tide of TB now appears to have turned in the United States. Nationally, new TB cases have been on the

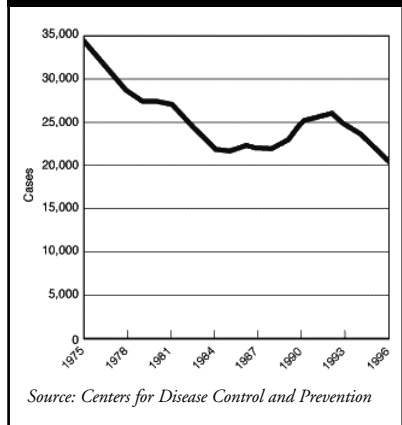
decline since 1992. In 1996, new TB cases fell to an all-time low of 21,337 cases, according to the most recent statistics from the CDC.

“The national TB control strategy has been very effective,” says Dr. Henry Francis, director of NIDA’s new Center on AIDS and Other Medical Consequences of Drug Abuse. However, rates of latent TB infection remain high among injecting drug users and in geographical pockets and have the potential for active disease and transmission, he notes. “It is important to maintain our vigilance, or we will see TB rates start to climb again,” he says.

Source

- Centers for Disease Control and Prevention. Tuberculosis morbidity United States, 1996. *Morbidity and Mortality Weekly Report* 46(30): 695–700, 1997. **NN**

Tuberculosis Cases Reported in the U.S. 1975–1996



After many years of declining, TB rates in the United States started to increase again in 1986, and accelerated into the early 1990s, peaking at 26,673 in 1992. Since then, new TB cases have declined, falling to an all-time low in 1996.

Interagency Pacts and NIH Collaborations Extend NIDA's Research Reach

By Neil Swan, *NIDA NOTES* Staff Writer

Teamwork with sister Institutes of the National Institutes of Health (NIH) and other Federal agencies is increasing the cost-effectiveness and extending the reach of NIDA's research.

In one current research collaboration, NIDA is a key participant in a broad new effort extending across several Federal agencies to examine the links among violence, crime, and drug abuse. Research focuses on a host of criminal, medical, and social problems that are often related to drug abuse. These problems include sexual and physical abuse of children, violence against women, teenage crime and violence, trends in public attitudes toward violence, and violence-related demands on the Nation's courts, prisons, and delivery of health services.

Called the Violence Initiative, the cooperative research enterprise involves more than 20 Federal agencies collaborating under an Interagency Agreement. Two departments spearhead the Initiative: the Department of Health and Human Services (HHS), with NIDA taking a lead role; and the Department of Justice, represented by its research agency, the National Institute of Justice (NIJ). NIJ conducts research to fight crime, improve criminal justice, and evaluate criminal justice programs.

The 3-year Interagency Agreement for violence-related research also involves the Department of Housing and Urban Development, which has an interest in crime and social issues in public-supported housing. Also participating are the Department of Education, the Centers for Disease Control and Prevention (CDC), and other NIH Institutes in addition to NIDA—agencies with diverse objectives but a common interest in violence, its causes, and its consequences.

The Initiative is formally named the Interagency Consortium for Research on Violence Against Women and Violence Within the Family. It allows NIDA and the other agencies to bridge the gap between two bodies of research—studies relating to drug abuse, drug addiction, and mental health and studies relating to social and criminal justice questions. The Initiative spans academic disciplines to make the benefits of NIDA's biological and behavioral drug abuse research—ranging from basic neuroscience studies to investigations of the cost-effectiveness of drug abuse treatment innovations—applicable to those agencies interested in the many drug-related aspects of violence.

The research interests of NIDA and NIJ frequently overlap. For example, NIJ is vitally interested in causes of recidivism—the return to jail of inmates who have committed new crimes since their release—says Dr. Donald Vereen, NIDA's representative to the founding interdepartmental group. Recidivism and other disruptive or criminal behaviors may relate to what research has shown are drug-induced changes in the brains of drug abusers, which may be associated with drug craving, explains Dr. Vereen, who is NIDA's special assistant to the Director for medical affairs. Thus, drug abuse research can help in designing inmate drug abuse education and treatment programs, he says. NIDA-funded research already has provided much of the impetus toward innovative “drug courts” that seek to address both criminal justice and addiction problems by striving to keep offenders enrolled in drug abuse treatment programs, he says.

The initial research findings under the Initiative have not yet been reported, but previous cooperation between NIJ and NIDA has already proved productive, says Sally Hillsman, NIJ deputy director. “For example, we have benefited greatly from the work of NIDA's Community Epidemiology Work Group [which monitors trends in drug use patterns in selected U.S. cities].”

After the agreement was signed in late 1995, the participating agencies called for research proposals relating to various aspects of violence. Ten projects have now been funded, all of them studying drug or alcohol abuse-related violence issues, according to Dr. Coryl Jones of NIDA's Epidemiology Research Branch, who is monitoring the projects. Sometimes the substance abuse factor in the violence studies becomes much more apparent as the project continues, she says. For example, one Initiative project is studying violence toward female care providers—wives and daughters—over age 55. As the project continues, researchers are finding strong evidence that drug and alcohol abuse by the women's mates or parents is an important factor in their victimization by violence, she says.

Planning for the \$1.8 million Violence Initiative evolved from policymakers' interest in the Violence Against Women Amendment to the Violent Crime Control and Law Enforcement Act of 1994. “Early on, NIDA Director Dr. Alan Leshner got involved. He pushed us to get people from agencies outside of NIDA to participate,” says Dr. Vereen.

The agencies are able to collaborate thanks to the Interagency Agreement, a formal contract that spells out terms and financial commitments for participant agencies. “The Interagency Agreement is tailor-made for broad cooperative efforts like the Violence Initiative,” says Dr. Vereen. “It’s good for research as an enterprise, and it’s good for science. It takes advantage of an existing infrastructure. All the participating agencies get something out of it.”

“The Interagency Agreement is a good tool for funding in situations when there is no handy grant mechanism,” says Carol Cornwell, a budget analyst in NIDA’s Program and Financial Management Branch, who manages the Initiative’s funds since NIDA was designated

“banker” for the collaborative operation. “Several of the Violence Initiative’s participating agencies do not have a grant-issuing mechanism. But they can participate in the Interagency Agreement, making funding contributions, and have a say in the type of research that is funded.”

NIDA is also involved in other Interagency Agreements, including collaborating with the State Department to improve drug abuse research in South America (see “NIDA Advances Drug Abuse Research in Andean Countries,” *NIDA NOTES*, September/October 1997). The Institute is also working with other NIH Institutes, the Department of Energy, and the Department of Veterans Affairs to develop improved “informed consent” policies to ensure that people participating in research are adequately informed of related ethical issues and risks to their health.

Interagency Agreements are only one way that NIDA teams up with fellow Federal agencies. There are also collaborations in which NIDA joins with other NIH Institutes to conduct mutually beneficial research. These collaborations have proven to be productive and beneficial, says Dr. Vincent Smeriglio of NIDA’s Clinical Medicine Branch.

NIDA currently is involved in four major collaborations with other NIH Institutes and public health agencies. In the **Maternal Lifestyles Study**, NIDA collaborates with the National Institute of Child Health and Human Development (NICHD), the HHS Administration on Children, Youth, and Families, and the Center for Substance Abuse Treatment. The agencies are studying the health and development of infants and children who are exposed to illicit drugs during their mothers’ pregnancies. More than 11,000 mothers were interviewed about their pregnancies and drug use, and some 1,400 infants are enrolled in followup studies. The continuing project is building valuable information for developing enhanced interventions to better address prenatal drug exposure and its possible consequences.

“The Interagency Agreement is tailor-made for broad cooperative efforts like the Violence Initiative. It’s good for research as an enterprise, and it’s good for science.”

The **Women and Infants Transmission Study (WITS)** is a six-site collaborative project studying mother-to-infant transmission of HIV. NIDA is collaborating with the National Institute of Allergy and Infectious Diseases (NIAID), the lead NIH Institute involved in HIV and

AIDS research, and NICHD. More than 1,200 HIV-infected women and 800 of their children have been enrolled. Approximately half of the WITS participants are current or former drug abusers. NIDA joined the collaboration to support and promote focused research regarding the impact of drug use on the transmission and course of HIV disease.

Reaching for Excellence in Adolescent Care and Health

(REACH) is an NICHD-initiated project with NIDA as a key collaborator. REACH seeks to learn more about HIV disease progression and its relationship to other health factors, such as drug use among adolescents aged 12 to 19. NIDA support emphasizes research on both the impact of drug use on the course of HIV disease as well as the impact of HIV on drug use. Also participating in the REACH collaboration are NIAID and the Health Resources and Services Administration.

The **Women’s Interagency HIV Study (WIHS)** and the companion **HIV Epidemiology Research Study (HERS)** investigate the medical and psychosocial impact of HIV on women. Most of the women being studied have a history of current or past drug use. The studies have enrolled 2,500 HIV-positive women and 775 HIV-free women. NIDA collaborates in these studies with NIAID, NICHD, the National Cancer Institute, the National Institute of Dental Research, and the CDC. NIDA funding supports research on how drug use and addiction may influence women’s vulnerability or resistance to HIV infection, the consequences of coinfection with HIV and other diseases associated with drug abuse, the effectiveness of HIV medical treatment, and biomedical factors related to the development of HIV disease.

“Each of these collaborations ensures that NIDA’s knowledge and expertise in drug abuse and related conditions are pooled with the knowledge of our colleagues in other Institutes and agencies conducting vital HIV research,” says Dr. Smeriglio. “It’s a highly cost-effective way to bolster NIDA’s clinical research and to expand interest in drug abuse issues among a larger pool of investigators.” Together with the Interagency Agreements, these collaborations broaden the consequences of NIDA research and extend NIDA’s science-based findings into new realms. **NN**

Contributions of Behavioral Research To AIDS Studies Recognized

By Neil Swan, NIDA NOTES Staff Writer

Behavioral and social sciences research is playing an increasingly critical role in the Nation's public health response to the spread of AIDS, according to experts at a National Institutes of Health (NIH) symposium last summer.

Dr. James Curran, an AIDS epidemiologist and professor at Emory University in Atlanta, said that science has made significant advances in recognizing the "previously marginal" role for behavioral studies related to AIDS. He spoke at the half-day symposium, Substance Abuse and AIDS: Research from the Behavioral and Social Sciences. The meeting at the NIH campus in Bethesda, Maryland, was cosponsored by NIDA.

AIDS is still a young epidemic, said Dr. Curran, formerly head of the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention (CDC) in Atlanta.

Early public responses tended to "ghettoize" those with AIDS, downplaying its spread into the general population through heterosexual contacts, he said. As a result, the public mistakenly has failed to recognize the importance of heterosexual contacts in the spread of HIV. Among women, particularly among poor and minority women, heterosexual sex is key to the currently increasing rate of HIV infections, he said. Statistics from the CDC support this view. In September, the CDC reported that the number of AIDS cases is increasing faster among women than among men and that sex with infected men has overtaken drug abuse as the leading cause of HIV infection among women. From 1991 through 1995, the number of men diagnosed with AIDS increased by 12.8 percent, versus an increase of 63 percent for women. However, many of the sex partners of these HIV-infected women are men whose own infections are drug abuse related.

Behavioral factors play an important part in these gender differences, say experts. Studies show that homosexual men, who now account for approximately 48 percent of all AIDS patients, are often well educated, aggressive about their treatment options, and responsive to prevention efforts. But many women with HIV are poor, are not well educated, and may have limited access to health care. As a result, these women may not respond as well as some men do to prevention or treatment efforts.

Behavioral studies are vital to learning more about the spread of the HIV infection, agreed Dr. William Paul, former director of NIH's Office on AIDS Research. After reviewing NIH-supported AIDS research, outside experts

recommended strengthening the social sciences and behavioral components of the research portfolio, advice now being heeded in NIH's AIDS research agenda, said Dr. Paul. NIDA ranks third among NIH Institutes in the level of funding it receives for AIDS studies, and much of the NIDA-supported research is already devoted to behavioral and social sciences investigations into the link between drug abuse and AIDS.

"AIDS and drug abuse are two epidemics that are totally intertwined," NIDA Director Dr. Alan I. Leshner reminded those attending the session. "It's impossible to speak about one and not the other. Behavioral and social science research is critical to gaining insights into the epidemiology of AIDS, and it helps the broader scientific community get a handle on this intersection of drug abuse and AIDS."

Studies of social and personal networks are vital to understanding HIV transmission and prevention, said Dr. Carl Latkin, a NIDA-supported researcher at Johns Hopkins University in Baltimore. "We need to look not so much at individual behavior but more at social-network aspects of behavior," he said. "We need to learn more about support networks that provide protection against HIV transmission and risk networks that actually promote high-risk behaviors."

Numerous studies have documented that significantly lower rates of HIV risk behaviors are practiced by drug abusers who are enrolled in treatment programs, said Dr. David Metzger, another NIDA-funded researcher at the University of Pennsylvania. "The consistency of these findings suggests that increasing the access to drug abuse treatment is a legitimate and absolutely necessary HIV prevention activity," he said. "Although the data [supporting the effectiveness of drug abuse treatment in preventing HIV transmission] are strongest for methadone treatment of opiate dependence, there also is growing awareness of the important role that noninjection drug use has played in the sexual transmission of HIV."

He noted that the protective effects of drug abuse treatment are not immediate and not universal. This underscores the need to investigate all modalities of treatment to document the effectiveness of each in changing behaviors to prevent HIV transmission. **NN**

"Increasing access to drug abuse treatment is a legitimate and absolutely necessary HIV prevention activity."

Other Drug-Use Paraphernalia Besides Needles May Increase HIV Infection Risk

Educating injecting drug users (IDUs) to reduce their risks of HIV transmission by using clean needles and by switching to other drug use practices may be communicating only part of the message necessary to effectively change high-risk behaviors, according to a NIDA-funded study.

The study is among the first to show that drug paraphernalia other than needles and syringes also may place IDUs at increased risk of HIV infection, according to Drs. Paul Shapshak, Syed Shah, and Clyde B. McCoy of the University of Miami and their colleagues, who conducted the study. The researchers detected evidence of the AIDS-causing virus in injection paraphernalia found in Miami “shooting galleries,” where drugs regularly are injected and traded, often in exchange for sex. Their evidence indicates that using contaminated water for rinsing needles, cotton swabs for filtering drug solutions, and “cookers” such as spoons or bottle caps for dissolving drugs possibly may be responsible for transmitting the AIDS virus.

The researchers used HIV’s distinctive genetic structure, its DNA, as a marker to detect its presence in the injection paraphernalia. They found evidence of HIV DNA in

up to 85 percent of contaminated needles collected from shooting galleries and in up to 36 percent of cotton swabs, 54 percent of cookers, and 67 percent of rinse water samples.

AIDS prevention efforts targeting IDUs have focused on encouraging them to clean their needles or to not swap needles, points out Dr. McCoy. This strategy implies that using clean needles eliminates the risk of HIV transmission when that may not be true, he warns.

“These drug users need to understand that all of the paraphernalia—the rinse water, cottons, cookers—are potential vehicles for transmission of HIV.”

Source

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CDC Report Highlights Link Between Drug Abuse and Spread of HIV

By Neil Swan, *NIDA NOTES* Staff Writer

An extensive review of existing research data confirms that behavior associated with drug abuse is the single largest factor in the spread of HIV/AIDS in this country. Half of all new infections with HIV, the virus that causes AIDS, now occur among injecting drug users (IDUs), according to the data review, which was conducted at the Centers for Disease Control and Prevention (CDC) in Atlanta.

The study focused on three groups recognized as being at highest risk for transmission of HIV: IDUs, men who have sex with men, and heterosexual men and women who are at risk because they have sex with IDUs and/or bisexual or gay men. The review used data gathered from America's 96 largest cities, where HIV infection rates are the highest in the Nation. The trends in HIV infection rates found in these cities also apply to the Nation's population in general, says the CDC reviewer Dr. Scott D. Holmberg.

Most newly HIV-infected IDUs live in northeastern cities from Boston to Washington, D.C., as well as in Miami and San Juan, Puerto Rico, reports the CDC reviewer. In these cities, where injection drug use rates are also the highest among the 96 cities surveyed, an average of 27 percent of all IDUs are HIV-infected.

"These data confirm and underscore the connection between injection drug use and the continuing spread of HIV and AIDS," says NIDA Director Dr. Alan I. Leshner. "Drug abuse and HIV are truly interlinked epidemics."

"The information further demonstrates that NIDA has a critical role indeed in addressing the drug abuse-HIV connection and in focusing scientific research to understand and deal with the further spread of this devastating disease," he says.

The data confirm earlier figures from periodic CDC reports on the number of newly diagnosed cases of AIDS and HIV infection, which suggested that the proportion of new HIV cases linked to drug abuse was close to one-half. (See "NIDA Plays Key Role in Studying Links Between AIDS and Drug Abuse," *NIDA NOTES*, May/June 1995, p. 88.)

Dr. Holmberg set out to estimate the size and direction of the HIV epidemic in major U.S. cities with populations greater than 500,000. He compiled a large computer model for tracking disease trends by reviewing more than 350 documents, several large research data sets, and information from 220 public health authorities. Some of the reports date back 10 or more years.

The 96 metropolitan areas Dr. Holmberg looked at have an estimated 1.5 million IDUs, 1.7 million gay and bisexual men, and 2.1 million at-risk heterosexuals. Among these three risk groups there are currently an estimated 565,000 HIV infections, with 38,000 new infections occurring each year. Using these data to make nationwide projections, the review concludes that there are about 700,000 current HIV infections, with 41,000 new HIV infections occurring each year in the U.S. population.

HIV Infections Among At-Risk Populations In America's 96 Largest Cities

Risk Group	Estimated Number in Risk Group	Estimated Percent HIV Positive	Estimated New HIV Infections Each Year Per 100 Group Members
Injecting Drug Users	1.5 million	14.0%	1.5
Men Who Have Sex With Men	1.7 million	18.3%	0.7
At-Risk Heterosexuals*	2.1 million	2.3%	0.5

* Men and women who are at risk because they have sex with injecting drug users and/or bisexual or gay men.

Chart shows percentages of at-risk groups in major cities who tested positive for HIV. Estimates were compiled in 1996.

An estimated 19,000 IDUs are infected each year in these 96 metropolitan areas, indicating an HIV incidence rate of about 1.5 infections per 100 IDUs per year, Dr. Holmberg reports. Infection rates are lower for the other two high-risk groups. Although gay and bisexual men still represent the group with the greatest number of current HIV infections, the rate of infection—except in young and ethnic/minority gay men—is much lower now than it was a decade ago, Dr. Holmberg reports. For gay and bisexual men, the HIV infection rate per 100 persons per year is 0.7; for at-risk heterosexuals—those who have sex with IDUs or gay and bisexual men—the rate is 0.5 infections per 100 persons per year. At-risk heterosexual women outnumber at-risk heterosexual men about 4 to 1.

In the research review, HIV incidence rates for metropolitan areas were broken down by estimated numbers of HIV-infected people in each of the three at-risk groups. An estimated HIV infection rate for each group in each city was also provided. “This is highly valuable epidemiological information for better targeting prevention strategies,” says Dr. Leshner.

“The HIV epidemic is now clearly driven by infections occurring among injecting drug users, their sex partners, and their offspring,” concludes Dr. Holmberg in his review. However, NIDA-funded efforts to educate IDUs to modify their risky drug use behaviors have proven effective, he says. Evidence shows that HIV infection rates

in injecting drug users have declined over the past several years in the largest drug-using communities, he reports.

In cities in New York and northern New Jersey, the epicenter of the AIDS epidemic among injecting drug users, many IDUs are switching to practices that may lessen their risk of contracting HIV, such as using sterile, never-used needles and syringes; cleaning needles and paraphernalia; sniffing rather than injecting heroin and cocaine; or abstaining from drug use altogether. This shows that drug abuse and AIDS prevention programs targeting IDUs are working, Dr. Holmberg says.

His review further illuminates the link between the AIDS epidemic and drug abuse as primarily a public health issue. Within this public health perspective, the CDC scientist’s review also provides important insights for policymakers, clinicians, and administrators who are planning and implementing drug abuse and HIV prevention and treatment programs. Targeting HIV treatment and prevention programs to IDUs also holds potential for reducing the spread of other blood-borne infections, including hepatitis B and C viruses.

Source

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NIDA Responds to the Changing Dynamics of the AIDS Epidemic

By NIDA Director Alan I. Leshner, Ph.D.

Drug abuse and the spread of HIV/AIDS, as well as other infectious diseases such as hepatitis and tuberculosis, are inextricably linked public health problems that require many and multifaceted solutions. A majority of new HIV infections in this Nation are related to drug abuse—through sharing of contaminated drug injection paraphernalia, through sexual contact with an injection drug user, or through the transmission of HIV perinatally. (See “CDC Report Highlights Link Between Drug Abuse and Spread of HIV,” *NIDA NOTES*, Vol. 12, No. 2.) NIDA has expanded its research efforts in this area to meet this challenge. The Institute has also set policies to ensure that all participants in NIDA-supported AIDS research are offered HIV testing and counseling.

NIDA-funded research has found that, through drug abuse treatment, prevention, and community-based outreach programs, drug abusers can change their behaviors.

They can reduce or eliminate drug use, drug-related HIV risk behaviors such as needle sharing, unsafe sex practices, and, in turn, the risk of HIV/AIDS. NIDA research also is working to reduce HIV and other AIDS-related illnesses and improve overall survival rates for

HIV-infected drug abusers by increasing their access and adherence to medical treatment. With a comprehensive research portfolio that is responsive to the changing dynamics of the AIDS epidemic, NIDA is improving the quality of life for many, as well as saving both lives and enormous costs to society.

NIDA-funded research has clearly shown that drug abuse treatment is highly effective in preventing the spread of HIV. Numerous studies have shown that individuals who enter drug abuse treatment programs reduce their drug use, which, in turn, leads to fewer instances of HIV high-risk behaviors.

NIDA's research into this field began early in the AIDS epidemic. One of the Institute's first investigations of drug use patterns among injection drug users (IDUs)—conducted in methadone treatment programs in New York City,

Philadelphia, and Baltimore—found that not only did participants report reduced sharing of needles, but also, 70 percent reported that they no longer injected drugs daily.

In addition to reducing injection drug use, individuals in drug abuse treatment programs have been found to have significantly lower HIV infection rates than drug abusers not in treatment. Researchers in Philadelphia compared HIV infection rates among drug abusers enrolled in methadone treatment programs to rates among those not in treatment. During the first 18 months of the study, those who remained out of treatment were nearly seven times more likely to have become infected with the AIDS virus than those in treatment. The investigators also found that the longer drug abusers remained in treatment, the less likely they were to become infected.

In aggregate, studies that look at abuse of drugs other than heroin and other injection drugs also are showing that drug abuse treatment lowers rates of HIV risk behaviors and infection. The bottom line is that providing access to effective drug abuse treatment programs is a proven way to prevent the spread of HIV/AIDS.

This is encouraging news. The discouraging news, of course, is that only a small percentage of those who need drug abuse treatment receive it. In fact, about 85 percent of chronic drug abusers are not in drug abuse treatment at any given time.

To reach that 85 percent, NIDA launched research to develop community-based outreach interventions to reduce the spread of HIV. The National AIDS Demonstration Research (NADR) Program was the first multisite research program to deliver and evaluate HIV risk reduction outreach programs to drug abusers not in treatment. As part of the interventions, outreach staff indigenous to the selected communities met with IDUs in their natural settings to distribute HIV risk reduction information and offer additional counseling and HIV testing. The outreach workers acted as credible messengers, provided risk reduction materials and education, and



***Drug abuse treatment,
prevention, and
community-based outreach
programs can change
behaviors to decrease
the risk of HIV/AIDS.***

arranged for IDUs to receive free, private HIV testing and counseling. The ongoing Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program uses similar behavioral interventions to reduce HIV risk taking and increase protective behaviors.

These programs and other NIDA-funded research have helped identify intervention models that enable IDUs to reduce their drug use, needle-sharing practices, unsafe sex behaviors, and, importantly, their HIV infection rates.

For example, a 4-year study at one of the first NADR projects in Chicago used ex-addicts to deliver HIV prevention services such as HIV testing and counseling. IDUs who were exposed to the intervention showed a significant decrease in the rate of new HIV infections. This is just one illustration of how outreach can help IDUs not in treatment change their HIV risk behaviors.

While we continue to fund research on interventions that change behaviors and prevent HIV transmission, we are also studying how to link HIV-infected drug abusers to the medical care they need for their HIV and related illnesses. Other NIDA-funded research is examining ways to increase drug abusers' compliance with medical treatment. Long-term studies are examining the influence of drug use on the progression of HIV and on the effectiveness of medical treatment.

We are also funding research that is examining the special needs of HIV-infected women who are drug abusers.

Unfortunately, with AIDS now being the fourth leading cause of death among women 15 to 44, the need is greater than ever to address the multitude of issues concerning this population. Among other things, NIDA-funded research is investigating the impact of drug use on maternal-infant HIV transmission, the course of the disease in drug-abusing women and their infants, and treatment with HIV medications to reduce transmission.

Given the public health implications of HIV/AIDS and drug abuse, NIDA must work to disseminate its research findings to the public health community at large. NIDA is teaming with the Centers for Disease Control and Prevention to reach their network of public health professionals in order to inform them what NIDA's research is showing about the inextricable link between these two diseases.

Despite substantial progress in HIV/AIDS prevention with drug abusers, unacceptably high numbers of new HIV infections are occurring in drug abusers, their sex partners, and their children. Many drug abusers still are engaging in high risk practices. To curtail or reverse this trend, NIDA will continue to build a comprehensive research portfolio that will respond to the changing dynamics of the AIDS epidemic. Equipped with the knowledge that drug abuse treatment, prevention, and community-based outreach programs can change behaviors to decrease the risk of HIV/AIDS, NIDA is in a position to develop the most innovative and effective programs possible through its research. **NN**

Drug Use During Pregnancy Associated With Increased Risk of Transmitting HIV to Infants

By Robert Mathias, *NIDA NOTES* Staff Writer

A national, multicenter study has found that HIV-infected women who used illicit drugs during pregnancy had a higher risk of transmitting HIV to their infants than did HIV-infected women who did not use drugs while pregnant.

The study, known as the Women and Infants Transmission Study (WITS), was launched in 1989 by the National Institute of Allergy and Infectious Diseases (NIAID) to track the natural history of HIV in infected women and their infants. The study currently is funded by NIAID, NIDA, and the National Institute of Child Health and Human Development.

In the study, researchers analyzed data on 530 HIV-infected pregnant women and their infants who were treated in obstetric and pediatric clinics in five cities across the United States. The analysis showed that the HIV perinatal transmission rate for women who used drugs during pregnancy was 27 percent compared with a 16 percent transmission rate among HIV-infected women who did not use drugs. Forty-two percent of the women in the study used illicit drugs during pregnancy; 44 percent of those women used multiple drugs. The most commonly used drug was cocaine, used either alone or in combination with other drugs.

The study's findings emphasize the critical role of drug abuse treatment in prenatal health care for HIV-infected

pregnant women who use drugs, according to Dr. Evelyn M. Rodriguez of the Health Resources Services Administration and her colleagues in the WITS. The WITS findings also underscore the importance of ensuring that all HIV-infected women receive information on how AZT (zidovudine) treatment during pregnancy can significantly reduce perinatal transmission of HIV, the researchers conclude.

Large multisite studies such as the WITS enable researchers to investigate both the behavioral and basic biological factors that may contribute to maternal-infant transmission of HIV, according to Dr. Vincent Smeriglio and Katherine Davenny of NIDA's Division of Clinical and Services Research, who are members of the WITS research staff. Further research is planned to verify the association between maternal drug use and infant HIV infection and to clarify the possible mechanisms of this association, they indicate.

Source

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Opioid Analogue May Slow Spread of HIV in Brain

By Neil Swan, NIDA NOTES Staff Writer

Synthetic compounds, or analogues, related to the opiates morphine and heroin can limit the growth of HIV—the virus that causes AIDS—in the brain, according to NIDA-funded research findings. The study with human cell culture suggests that a synthetic compound that binds to the brain's kappa opioid receptors (KOR) may curtail a virus subtype called HIV-1 from spreading in the brains of people infected with the AIDS virus. A drug analogue is a chemical compound that differs slightly from another drug.

Although the study was performed in cell culture, the results suggest the possibility that a medication could be developed to prevent a particularly destructive aspect of AIDS—the loss of intellectual capacity. This research is part of a broad range of NIDA-supported studies of the complex relationship between drugs of abuse and AIDS, including studies of the effects of drug use on the body's immune system and, subsequently, on infection and disease progression. The study also provides an example of how research on drugs of abuse can have benefits in other areas of medicine.

In some HIV-infected patients, HIV-1 infection in the brain leads to a disease syndrome called "AIDS dementia complex," which results in apathy, difficulties in muscle control and movement, and problems in performing complex tasks. The mental capacity of patients with dementia complex may deteriorate until they are incapable of voluntary acts.

When HIV-1 involves the brain, the infection occurs in microglial cells, found throughout the nervous system, which are the principal sites for HIV growth in the brain.

The study was conducted by Drs. Chun C. Chao and Phillip K. Peterson and their colleagues at the Minneapolis Medical Research Foundation and the University of Minnesota Medical School. It builds on research by Dr. Jean Bidlack of the University of Rochester Medical School in New York and the late Dr. Sydney Archer of Rensselaer Polytechnic Institute in Troy, New York.

Dr. Chao says the collaboration developed at a NIDA-supported symposium on interactions between drugs of abuse and the immune function.

To learn more about these interactions, the Minnesota scientists first treated microglial cell cultures with two KOR agonists—compounds that mimic actions of the body's natural kappa opioids—for 24 hours and then infected the treated cells with HIV-1 for another 24 hours. When the researchers examined the cell culture after 14 days, they found that pretreatment with the KOR agonists U50,488 and U69,593 prevented the growth of HIV-1. Currently, they are testing other synthetic KOR compounds for their potential for treating AIDS dementia complex.

The next step will be to conduct similar studies on the effect of KOR compounds on the spread of HIV in living animals, says Dr. Chao. Some of these studies likely will examine the growth of simian immunodeficiency virus (SIV) infections. SIV is an HIV-like virus found in monkeys. "One possibility is to treat SIV-infected monkeys with kappa opioid compounds, such as those we used in the human

cell culture study, to test whether these KOR compounds have therapeutic value in monkeys with SIV," Dr. Chao says.

Dr. Chao presented his findings at the Fourth Annual Symposium on AIDS, Drugs of Abuse, and the Neuro-Immune Axis held in conjunction with the annual meeting of the College on Problems of Drug Dependence in San Juan, Puerto Rico, in June. Scientists at the symposium concentrated on both human and animal data to study the relationships among drug abuse, immune function, and infectious diseases.

Both human and animal studies show that different drugs and different classes of opiates regulate the immune system function in different ways. For example, earlier findings by Dr. Chao and his colleagues show that in human cell culture morphine, unlike the KOR agonists, may stimulate growth of HIV in microglia.

This research is part of a broad range of NIDA-supported studies of the complex relationship between drugs of abuse and AIDS, including studies of the effects of drug use on the body's immune system.

Likewise, a particular drug may regulate the human immune system differently than it does an animal's immune system. Sometimes drug-induced influences on immune function increase the death rate of animals with infectious disease.

A study by Dr. M.P. Yeager at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire, on the acute effects of morphine on humans did show that morphine caused marked immune suppression. But epidemiologic research has provided only limited evidence of similar findings.

While some epidemiologic studies indicate that injecting drug users (IDUs) are at increased risk for infection with tuberculosis and HIV, natural history studies can find no evidence that HIV infection progresses more rapidly among IDUs than among other risk groups, including people who do not abuse drugs: both homosexuals and heterosexuals. Other research also suggests that some drug abusers may be more susceptible than are people who do not abuse drugs to "opportunistic" infectious diseases, such as pneumonia, that may arise after physiological damage or weakening of the immune system by AIDS. The basis of this apparent susceptibility is not clear.

"You can find drug-induced effects in test-tube experiments and in animals that you can't duplicate in humans," says Dr. John Madden of Emory University in Atlanta, cochair of the symposium. "In the test tube and in animals, researchers are usually testing the short-term, acute effects of drugs on the immune system and disease progression. But in humans addicted to heroin, they are more often dealing with long-term, chronic drug effects. It appears that addicts build up a state of homeostasis in which the immune system over time adapts to the effects of the drugs and returns to an apparent state of normalcy." He notes that this state of apparent normalcy can be disturbed, however, by stresses such as drug withdrawal, infectious diseases, or poor nutrition.

Researchers are seeking to develop a research model in monkeys that more closely resembles the chronic effects found in human addicts, says Dr. Madden. They are also focusing more on other variables, such as the effects on the immune system of stress induced by drug withdrawal, and the relationship between drug use and disease susceptibility in the early stages of addiction.

In some HIV-infected patients, HIV-1 infection in the brain leads to a disease syndrome called "AIDS dementia complex," which results in apathy, difficulties in muscle control and movement, and problems performing complex tasks.

Inconsistencies between laboratory animal findings and epidemiologic data on the effect of drugs of abuse on the progression of AIDS in humans may result from a number of other factors, researchers say. These include the overall health status of drug-abusing individuals, which can vary significantly among different drug-using groups; difficulty in tracking injecting drug users over time; and the possibility that the death or serious illnesses of some study subjects may go unreported when they are instead counted as study "dropouts." In addition, polydrug abuse may have com-

pounding or even conflicting effects since there is evidence some drugs of abuse may actually counteract the immune system effects of other drugs. Researchers have noted that many HIV-infected people studied use both heroin and cocaine, which may have opposing or conflicting effects on immune system regulation and, perhaps, on AIDS disease progression.

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Drug Abuse Links to AIDS Prompt Highly Targeted Responses

By Neil Swan, *NIDA NOTES* Contributing Writer

NIDA-supported research to prevent the spread of AIDS related to drug abuse is building on what has been learned from an array of prevention approaches that target specific populations and selected high risk drug-use and sexual practices. At the same time, basic research sponsored by the Institute is probing factors associated with the dual epidemics of AIDS and drug abuse, including the role of drug use in the rate of disease progression to AIDS following exposure to HIV, the human immunodeficiency virus, which causes AIDS.

Presentations at two recent NIDA conferences on AIDS and drug abuse reflect the profound role drug abuse plays in the spread of HIV. (See "NIDA Plays Key Role in Studying Links Between AIDS and Drug Abuse," *NIDA NOTES*, May/June 1995.) The conferences were held last summer in Scottsdale and Flagstaff, Arizona.

"We're learning what works for whom" in interventions to reduce the risk of infection with HIV, explains Dr. Richard H. Needle, chief of the Community Research Branch in NIDA's Division of Epidemiology and Prevention Research.

"The cumulative research literature can be examined for indications of progress," says Dr. Needle, whose branch helped sponsor the Flagstaff meeting. "Each individual study has strengths and limitations, but, collectively, generalizations can be drawn. We see where we have been effective and we learn how to be even more effective" in curtailing behaviors that put people at risk of contracting or transmitting HIV.

"These conferences were extremely useful in bringing researchers together, involving other agencies, and sharing important data that have not yet been published," says Dr. Harry W. Haverkos, director of NIDA's Office on AIDS, which sponsored the Scottsdale meeting.

Drug Injection and AIDS Prevention

One conference presentation examined "sociometric and personal networks" of street injecting drug users (IDUs). These risk networks consist of a limited number of core users whose network standing and prominence may influence drug use practices of others at the network fringes. The NIDA-funded study queried 687 street-recruited injecting drug users in New York City about their drug use and sexual behaviors. Researchers identified two network variables as significant predictors of HIV infection:

being a core network member and having an older IDU in one's personal network.

Drs. S.R. Friedman and A. Neaigus of National Development and Research Institutes, Dr. D.C. Des Jarlais of Beth Israel Medical Center, and their colleagues in New York City concluded that future prevention efforts for street IDUs should target core network members and address factors leading to core group membership as well as injection practices among groups of users of different ages and experiences.

Among emerging intervention approaches are those that target groups with dual risks for acquiring HIV. Men who have sex with other men and also inject drugs engage in two high-risk behaviors. They can serve as a "bridge" linking others who belong to one of these two high-risk populations. In many western states, this dual-risk category was identified in as many as 50 percent of HIV cases.

Programs are under way in Seattle, San Francisco, and Los Angeles to target this bridge population composed of both HIV-infected and uninfected persons. Innovative interventions to counsel, educate, and reduce behavioral risks are proving effective, according to several measures. They result in less needle sharing; reduced frequency of drug use; increased knowledge about unsafe sex practices, sexually transmitted diseases, and HIV; and improved compliance with tuberculosis and HIV medication regimens, according to a NIDA-funded grantee, Dr. Michael Gorman of the University of Washington. Injecting drug using men who have sex with other men "represent a critical, hidden, heretofore underserved, poorly understood population" that can benefit from innovative public health prevention interventions, he reported.

A similar NIDA-facilitated study describes HIV prevention interventions that target men who have sex with men and who use methamphetamine. HIV prevention efforts in Seattle, San Francisco, and Los Angeles—cities with a high prevalence of AIDS among men who have sex with men and methamphetamine use—are being studied.

Another analysis of Seattle's needle-exchange program examined IDUs who regularly pool their pocket money to buy drugs. The study found a link between pooling money for drugs and high-risk practices like the sharing of needles and drug paraphernalia. "It may be worthwhile to target prevention efforts at this clustering of risk around the joint purchase of drugs," reported Dr. James McGough of the King County, Washington, Health Department.

Drug Abuse Treatment

Several studies and analyses presented at the two conferences further document the effectiveness of drug abuse treatment in reducing drug use, crime, and HIV infection.

Data on AIDS risk behaviors of some 10,000 drug abuse treatment clients from 1991 to 1993, collected by NIDA's Drug Abuse Treatment Outcome Study, were analyzed by Dr. Wendee M. Wechsberg and others of the Research Triangle Institute and NIDA. The patients, from 99 treatment programs, reported that behaviors putting them at risk of HIV infection needle sharing, sex with multiple partners, and unprotected sex were reduced somewhat during treatment. Researchers suggest this large-scale survey validates findings of smaller studies, demonstrating the benefits of drug abuse treatment and emphasizing the importance of AIDS prevention interventions during treatment.

While drug abuse treatment is generally recognized as effective in reducing HIV risks among those in treatment, the impact of effective treatment extends beyond treated individuals and into their social networks, research indicates. Recent studies in the Philadelphia area suggest that treatment not only reduces the frequency of injection drug use but also changes patterns of use. Individuals in treatment report less injection drug use with strangers and acquaintances. There is a corresponding increase in the number of individuals who report always using drugs alone. Treatment thus has the effect of removing links in drug-using networks and reducing the risk of spreading HIV through those networks. In reducing drug use with others, treatment's "role in tertiary prevention is significant and perhaps under-appreciated," concluded Dr. Martin Y. Iguchi of the Medical College of Pennsylvania and Hahnemann University.

Basic Research on Drug Abuse and AIDS

A number of NIDA-funded basic science investigations examining the relationship between drugs of abuse and the functions of the immune system were presented at the conferences.

Previous research had found evidence that drugs of abuse can suppress the immune system in laboratory animals. But scientists have not demonstrated the clinical impact in humans. It is, therefore, important to select and use appropriate laboratory animal models of HIV infection and progression patterns in humans.

Research by Dr. Lisa H. Gold and colleagues at the Scripps Research Institute demonstrates that neurobehavioral abnormalities in rhesus monkeys and cats infected with viruses similar to HIV (simian and feline immunodeficiency viruses) and in certain genetically engineered

mice make these animals suitable experimental models for future studies of the interactions between drugs and HIV. Cognitive testing partially supported by NIDA, along with other neurological assessments, indicates that monkeys infected with the simian immunodeficiency virus undergo nervous system changes similar to those seen in HIV-infected human patients.

Another study examined the effects of morphine on the immune status and disease resistance of monkeys infected with the simian immunodeficiency virus. The study found that the effect of opiates on the immune system may be variably and conditionally dependent on whether the drug doses are long-term and steady or sporadic, with sporadic dosing having less apparent effect. The NIDA-supported study was conducted by Robert M. Donahoe and colleagues at Emory University and Dr. Mario Aceto of the Medical College of Virginia.

Evidence shows that opiates play a role in modulating HIV infection in the brain, according to another study by Dr. Chun C. Chao of the University of Minnesota and others. They found that an artificial compound called U50,488 that binds selectively to the kappa opioid receptor markedly suppresses HIV cell reproduction in the brain, where the deadly virus usually replicates.

Other AIDS and HIV Prevention Research

More than 100 oral presentations were given and scores of scientific abstracts were displayed at the NIDA conferences, including those with these findings:

- Although drug use itself was not found to be associated with mother-to-child HIV transmission in the women studied, drug users had poorer prenatal care, more adverse birth outcomes, and many clinical characteristics like increased rates of anemia, pneumonia, and smoking that may increase the possibility of HIV transmission to their newborns.
- Interventions with out-of-treatment heroin addicts are more successful when they include actual scheduling of treatment admission instead of simply distributing lists of treatment centers. This active referral results in higher treatment rates, and those persons entering treatment are more strongly associated with reduced drug use and less criminal activity.
- Research on community outreach for HIV prevention in mid-sized towns determined that adding two sessions to a "standard" office-based counseling program led to additional reductions in HIV risks in Flagstaff, Arizona, as reported by Dr. Robert Trotter of Northern Arizona University. **NN**

Treatment and Outreach Research on AIDS: Identifying and Treating Those at Risk

By Neil Swan, *NIDA NOTES* Contributing Writer

NIDA's drug abuse treatment and outreach research is taking the Institute's AIDS prevention mission onto the front lines of the battle against HIV infection. NIDA-supported researchers in these programs work face to face with drug abuse populations to learn and implement more effective ways to reduce the risk of contracting HIV and AIDS. An important component in both treatment and outreach programs has been the search for ways to reduce HIV risks related to drug-injection practices.

Treatment Research

NIDA's years of experience in developing and implementing drug abuse treatment programs have enabled the Institute to identify, study, and modify drug-use behaviors that increase HIV transmission risks among people who are in treatment.

The Institute's AIDS-related treatment research has three major goals: improving therapies and getting more addicts into treatment, integrating effective HIV risk-reduction tactics into existing treatment programs, and designing treatment and services for targeted at-risk subgroups. These subgroups include gay men who are also drug users, women who don't abuse drugs but who have sex with men who do, HIV-positive addicts, and drug abusers who are in prison or are otherwise involved with the criminal justice system.

NIDA-funded studies have shown repeatedly that injecting drug users who are in treatment programs are less likely to engage in high-risk sexual and drug-using behaviors than are comparable addicts who are not enrolled in treatment. For example, a 1988 study of methadone treatment programs for heroin addicts found that comprehensive drug abuse treatment is effective in reducing injection drug use and needle sharing among most heroin addicts.

Subsequent NIDA-funded studies have reinforced these initial findings. University of Pennsylvania researchers studying heroin addicts in Philadelphia found that out-of-treatment subjects were injecting drugs, sharing needles, visiting shooting galleries, and practicing unsafe sex at significantly higher rates than in-treatment subjects. The 1993 study found that the addicts who did not receive treatment had a conversion rate to HIV-positive status that was *six times higher* than the rate among in-treatment injecting drug users who had been regularly exposed to



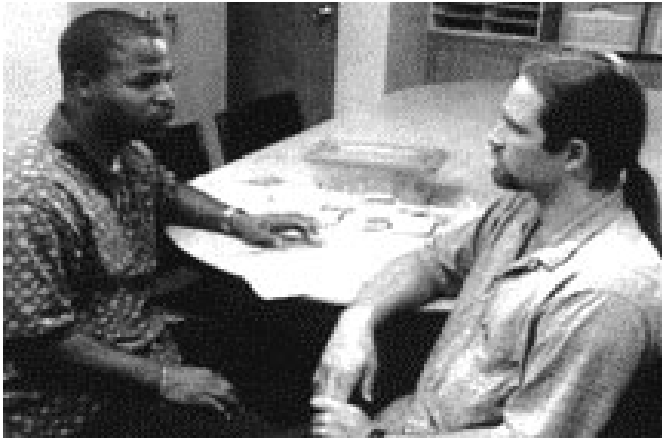
Case Manager Andrea Coward (left) listens to a client describe his life in a culture of drug abuse. "Hearing themselves say things to another person, a light bulb will go on, and it helps them realize what they can do to help themselves," Ms. Coward says.

risk-reduction education, counseling, and other strategies.

Unfortunately, HIV risk-reduction education and counseling, HIV testing, and AIDS risk behavior assessments have not yet been assimilated into many existing treatment programs for heroin and cocaine addicts. In response, NIDA is encouraging researchers who are developing and testing behavioral therapies for drug abuse and dependence to also develop HIV risk-reduction interventions that can be readily incorporated into existing drug-abuse treatment programs.

The Institute's behavioral therapies development program announcement has recently been expanded to specifically encourage behavioral research to develop HIV risk-reduction interventions. The program will identify, test, and introduce new behavioral therapies for drug abuse that ultimately can be used in community treatment clinics. Researchers will develop behavioral counseling, cognitive therapies, and other types of treatment designed to reduce the risk of HIV infection and will explore ways to improve treatment compliance, keep potential dropouts enrolled, and appeal to those who resist treatment.

Another new effort will seek to expand basic behavioral research to develop models of behavior and behavior



Counselor James Gaines (left), Community Outreach Program in Long Beach, California, discusses risk reduction with patient. NIDA-funded studies show that injecting drug users in treatment programs are much less likely to engage in high-risk sexual and drug-using behaviors than are comparable users not in treatment.

change relevant to HIV risk. These will include psychological, social, and biological approaches to explain and predict HIV-related behaviors among persons and groups in various settings. A significant aspect of this initiative will bring together researchers from different disciplines in a collaborative way to integrate scientific approaches in order to develop novel ways to address the HIV/AIDS problem.

Outreach Programs

Two landmark outreach programs, initiated by NIDA's Community Research Branch in collaboration with researchers around the country, have set the standard for investigations that shoulder the dual responsibility of AIDS prevention and drug abuse outreach and treatment.

The National AIDS Demonstration Research (NADR) Project, conducted from 1987 to 1992, funded 29 community-based HIV-prevention programs for out-of-treatment injecting drug users and their sexual partners. The followup Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program, launched in 1990, is currently evaluating the effectiveness of NADR intervention programs among different populations in different communities across the Nation, as well as looking at ways to expand the programs. As the examples cited below clearly illustrate, the interventions for out-of-treatment drug users undertaken in both programs accomplished statistically significant and clinically meaningful decreases in HIV-related risk behaviors.

NADR lived up to its description as an outreach program, reaching thousands of out-of-treatment drug users and their sexual partners during its 5-year life span. Reductions in risk behavior, from initial assessment to

followup assessment at 6 months, were striking and encouraging. Followup data revealed that 46 percent of NADR participants reduced or stopped injecting drugs, 37 percent reduced or stopped sharing needles, 50 percent reduced or stopped borrowing needles, and 60 percent reduced or stopped sharing other injection equipment. In addition, a substantial minority of injecting drug users underwent treatment after intervention, many for the first time in their lives.

Although changes in high-risk sexual behaviors were less marked than changes in drug-use behavior, they did show substantial improvement. For example, the proportion of injecting drug users who always used condoms increased from 10 percent before intervention to 19 percent afterward. The decrease in the percentage of subjects who reported having two or more sexual partners dropped from 44 to 36 percent.

The Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program continues NADR's goals of preventing the further spread of HIV infection among drug users and their sexual partners. Like NADR before it, the program uses street-based, face-to-face outreach and risk-reduction interventions and pretest and posttest HIV antibody counseling. The Cooperative Agreement takes NADR's research one step further, with controlled experimental research. Specific, well-defined populations have been recruited for intervention at multiple sites, and a standardized intervention is being used. The Cooperative Agreement is currently the only system of its kind that captures epidemiologic information on hard-to-reach, out-of-treatment drug-using populations.

As with research results from NADR, results from the Cooperative Agreement reveal a remarkable success story in reducing HIV risk behaviors. Examples of changes in risk behavior, from initial assessment to followup assessment at 6 months, include:

- a 41 percent reduction in frequency of injection, from 64 times in the past 30 days prior to intervention to 38 times in the past 30 days after intervention;
- a 54 percent reduction in reusing other persons' syringes, with 17 percent reusing another person's syringes before intervention and 8 percent at followup; and
- a reduction from 22 percent to 14 percent in the proportion of sexual partners who injected.

Outreach approaches are still being developed and evaluated. As the epidemiologic characteristics of the epidemic continue to change, becoming increasingly concentrated in hard-to-reach populations and subgroups, new techniques for monitoring the extent of HIV disease prevalence and for delivering effective interventions are critical in developing effective prevention strategies. NIDA is now

funding new epidemiology studies to better define the communities and demographic subgroups in which HIV is spreading, to further identify the specific behavioral risk factors related to the spread of HIV in each subgroup, and to evaluate what has been learned about using effective risk-reduction messages tailored to the needs of these subgroups. Research will concern the unique health care needs of high-risk populations of drug users, seeking ways to better meet their medical and social service needs.

Needle Exchange and Hygiene

NIDA has taken the lead in fighting the spread of AIDS among injecting drug users by studying various strategies to reduce HIV risks related to needle use.

One such study, the first federally funded needle-exchange evaluation, tracked the use of syringes among injecting drug users in New Haven, Connecticut, over 3 years. Data from the locally operated project, which includes HIV testing and medical monitoring, show that after the needle-exchange service was provided, the proportion of needles that tested positive for HIV dropped significantly. Using these data, the New Haven researchers estimated that there would be a 33 percent reduction in new cases of HIV infection among injecting drug users as a result of the needle-exchange program. Significantly, they also have reported that 17 percent of the study subjects have been referred to drug abuse treatment. NIDA is now funding similar evaluations in six other cities.

NIDA's multisite observation of needle hygiene practices among injecting drug users in 1993 provided information about another HIV risk involved in injection drug use—indirect sharing, which can occur when water or cookers used to mix drugs, cotton swabs, or a drug solution that contacts the bleach of one injecting drug user is used by another in the process of preparing or injecting drugs. Indirect sharing also can occur with the transfer of drugs from one syringe to another before injection.

NIDA researchers' data show that, despite reductions in the frequency of syringe sharing among users, indirect sharing remains a common practice, and some high-risk subgroups have not yet been targeted for risk-reduction interventions.

NIDA research in the 1980s suggested that common household bleach is more effective than most other readily available solutions such as alcohol and hydrogen peroxide in disinfecting needles and syringes used by injecting drug users. Bleach soon became the standard for use in needle hygiene programs, and small bottles of bleach and other HIV risk-reduction educational materials were widely distributed by outreach workers throughout the country. Because of wide disparities in bleach disinfection techniques by drug users, in 1993 NIDA issued a Director's Alert and later joined with the Centers for Disease Control and Prevention and the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment in issuing a bulletin on the most effective bleach disinfection procedures and urging the use of new or sterile equipment.

Now NIDA is recruiting researchers for a second generation of studies to examine strategies used in different injection risk-reduction projects—counseling, education, the crafting of messages targeting specific subgroups, linkages to drug treatment, and other variable components.

Sources

- National Institute on Drug Abuse. *Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program, 1990–Present*. Rockville, MD: NIDA, 1995.
- National Institute on Drug Abuse. *Outreach/Risk Reduction Strategies for Changing HIV-Related Risk Among Injection Drug Users*. NIH Publication No. 94-3726. Rockville, MD: NIDA, 1994. **NN**

NIDA Urges HIV Counseling, Testing for Research Subjects

Because of the strong link between drug abuse and the transmission of HIV, NIDA-funded researchers are strongly urged to provide HIV risk-reduction counseling and access to HIV antibody testing to individuals who are participating in NIDA-supported study projects. In announcing the policy, NIDA Director Dr. Alan I. Leshner pointed out that HIV risk-reduction interventions have been shown to be effective in reducing drug abuse-related behaviors that heighten the risk of spreading HIV.

The policy applies both to NIDA-funded programs for community outreach and intervention and to research conducted in clinics, hospitals, or clinical laboratories that involves ongoing contact with persons at risk for HIV infection. Those considered at risk include injecting drug users, crack cocaine users, and sexually active drug users and their sexual partners.

“Given the tremendous impact of the AIDS epidemic and the significant role of drug abuse in the transmission of HIV, NIDA has developed a policy to help reduce HIV risk behaviors and infection in drug-using populations, their sexual partners, and their children,” said Dr. Leshner.

HIV risk-reduction counseling includes education about HIV and AIDS, the behaviors that transmit HIV, and how to reduce the risk of transmission. Counselors also encourage individuals to have their blood tested for HIV.

Current grantees are encouraged to implement the policy as soon as possible. NIDA will use this policy when considering requests for supplemental funding of ongoing projects. **NN**

NIDA Plays Key Role in Studying Links Between AIDS and Drug Abuse

By Neil Swan, *NIDA NOTES* Contributing Writer

Since AIDS was first identified in 1981, the disease has brought death and widespread physical and social devastation to people and nations worldwide. An estimated 1 million Americans today are infected with HIV, the human immunodeficiency virus, which causes AIDS; as many as 17 million people are infected worldwide. According to the Centers for Disease Control and Prevention (CDC), 441,528 cases of full-blown AIDS were reported in this country through the end of 1994. Of these, approximately 60 percent have died.



Injection drug use was the second leading cause of new AIDS cases through mid-1994.

HIV infection is now the leading cause of death among Americans ages 25 to 44, according to the CDC. The transmission of HIV from women to their newborn infants is also a growing problem.

The critical connection between drugs and AIDS has become increasingly evident. Injection drug use was the second leading cause of new AIDS cases through mid-1994, accounting for 31.8 percent of all cases, according to the CDC (see chart).

One analysis based on current CDC data concluded that more than half of the 40,388 new HIV infections in 1994 were drug related. Groups at extremely high risk of infection include injecting drug users who share needles and other drug-use paraphernalia as well as crack addicts who

engage in unprotected sex with multiple partners. Also at high risk are sexual partners and offspring of these drug abusers.

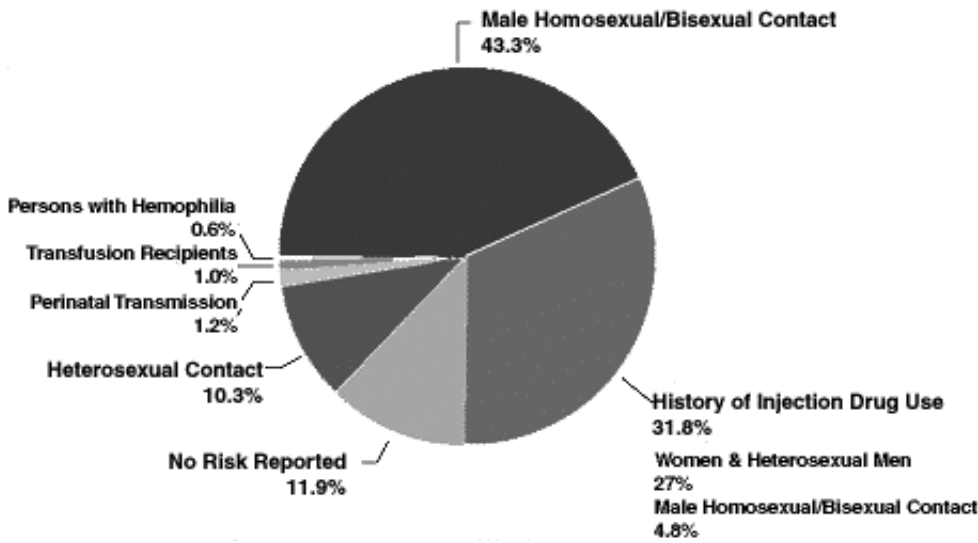
Because of this crucial link between AIDS and drug abuse, NIDA has played a critical role in the Government's strategy to control the spread of AIDS since early in the epidemic. Today, with a budget of \$147 million for AIDS-related research, NIDA is the third largest supporter of AIDS research among the 17 Institutes of the National Institutes of Health. One-third of NIDA's research funding is committed to studying AIDS.

For its AIDS research agenda into the 1990s, NIDA has taken its lead from the 1988 Charlottesville, Virginia, conference of the Public Health Service's leading AIDS experts, who coordinated a major public health response to the epidemic. The Charlottesville meeting set a number of public health goals relating to the drug abuse population: increasing the number of drug abuse treatment slots for injecting drug users; improving the quality and effectiveness of drug abuse treatment; recruiting and training drug abuse treatment specialists; increasing outreach and education efforts for injecting drug users and their sexual partners; and conducting research to clarify the extent, nature, and natural history of injection drug use and needle sharing, with special attention to cultural and ethnic differences in drug-related practices and behavior.

To advance those goals, NIDA has supported a broad agenda of research into AIDS-related drug-use behaviors and HIV risk-reduction interventions. Central to these efforts have been studies to improve drug abuse treatment and outreach strategies to reduce injecting drug use and related risk behaviors. Other NIDA studies have monitored the natural history and epidemiology of HIV and AIDS; explored basic research areas such as immunology and neuropharmacology; examined the needs of special populations such as women, children, and racial and ethnic minorities; and enhanced medical care and services to improve the lives of those who are HIV infected.

NIDA's research findings have resulted in major advances toward curtailing the spread of AIDS. Research has shown that comprehensive drug abuse treatment programs can be effective in reducing high-risk HIV behaviors. For addicts not in treatment, community-based street outreach (prevention and intervention) programs have been

Reported U.S. AIDS Cases by HIV-Exposure Category—1994



Source: Centers for Disease Control and Prevention, *Morbidity and Mortality Weekly Report*, Vol. 44, No. 4, Feb. 3, 1995

effective in recruiting hard-to-reach crack smokers and injecting drug users and in educating and motivating them to change high-risk drug-use practices and sexual behaviors. Basic and clinical research has provided vital information on the origin and development of drug-related HIV and AIDS.

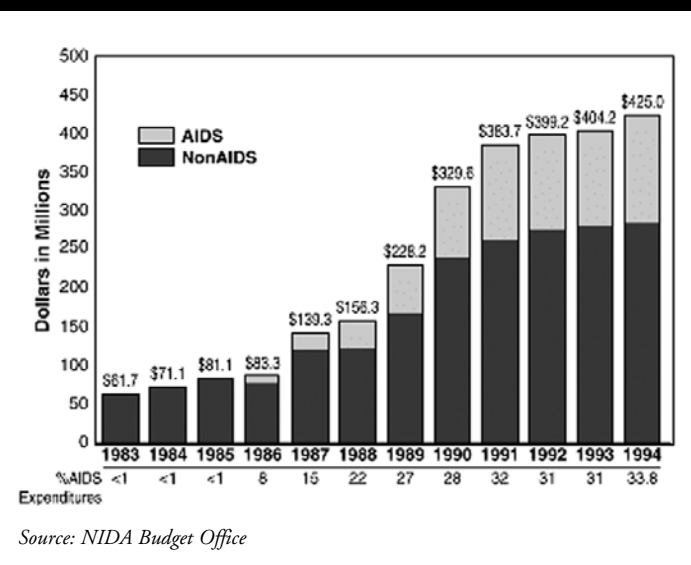
The challenge for NIDA now is to build on the advances already gained, fostering further research to unravel the intricate secrets of AIDS and designing improved interventions to bring this epidemic under control. To meet

this challenge, NIDA in 1993 adopted a 5-year strategic plan for AIDS research to learn more about reducing the transmission of HIV among drug users, their sexual partners, and their children. The plan has six elements:

- to conduct research to improve existing treatment approaches and develop pharmacologic and nonpharmacologic therapies;
- to carry out research to improve educational and behavioral strategies, including studies on outreach approaches, prevention and early diagnosis, and treatment of drug abuse;
- to undertake natural history studies of drug abusers, studies of drugs as potential cofactors in HIV disease, and basic and clinical immunological studies;
- to conduct seroepidemiological studies of drug abusers, studies of the nature and extent of at-risk drug-use and sexual behaviors (such as the “sex-for-crack” phenomenon), and ethnographic studies;
- to swiftly disseminate research findings and technologies using conferences, publications, and mass media campaigns; and
- to make recommendations to policymakers on strategies to counter the spread of AIDS and to establish close liaison with other AIDS research programs.

Building on its past research and the potential for improved AIDS prevention strategies, NIDA is now inviting scientists to join its efforts in devising innovative AIDS research initiatives that build on and extend prior NIDA-funded research. A broad range of basic and clinical research pathways, behavior-changing strategies, and drug-related variables are candidates for study. Investigators who can demonstrate the relevance of their proposed AIDS-related research to drug abuse are eligible to seek NIDA funding. **NN**

NIDA's AIDS and NonAIDS Expenditures



Source: NIDA Budget Office

Basic and Clinical Research on AIDS: From the Molecule to the Patient

By Neil Swan, *NIDA NOTES* Contributing Writer

Both NIDA's basic research and clinical research programs explore ways drugs of abuse affect the spread of HIV and AIDS. Studies funded under these programs range from complex molecular-level investigations to human studies.

Basic Research

Immunopharmacological research on drugs of abuse already has advanced understanding of the origin and development of drug-related HIV infection and AIDS. This research is accumulating evidence to indicate that opiates, marijuana compounds, and other drugs of abuse can suppress or enhance the immune system in laboratory animals.

Based on these findings, researchers supported by NIDA's Division of Basic Research are studying the complex interactions between the nervous system, where drugs of abuse have long been known to act, and the immune system, where recent studies show they act as well.

Several studies are exploring how opiates and other drugs modify or weaken immune defenses, alter neural capacity, and increase the potential for dementia. Neuroscientists have found that glial cells—the nonneuronal supporting cells in the brain and nervous system—help to modulate the immune defense against infection and are a primary focus of neuronal injury after infection.

Studies by NIDA-funded researchers have shown that opioids (morphine and naturally occurring morphine-like compounds) act on these glial cells to regulate this damage to the neurons in the brain.

One avenue of research is examining the ability of a specific protein on the surface of the HIV to activate certain neuron-damaging cytokines, the immune system's regulating neurotransmitters. NIDA-supported researchers have found that morphine and dynorphin, a compound similar to morphine that occurs naturally in the human body, enhance the ability of these HIV-activated cytokines to destroy human brain cells. This research holds promise for the development of new therapies for HIV-related brain diseases and HIV infection, as well as for brain injuries that are aggravated by inflammation.

Basic research suggests that opioids may suppress immune function by modulating the levels of these cytokines. The effectiveness of macrophages—large cells that circulate in

the blood destroying disease microorganisms—is reduced by both infection and opioids, causing either an increase in the production of destructive cytokines or a decrease in the levels of beneficial cytokines.

Morphine, for example, appears to enhance the progression of infectious pneumonia by reducing the number of macrophages in pigs, whose immune systems closely resemble those of humans. In contrast, it appears that the progression of encephalitis may be slowed by opioids.

Another NIDA-funded study showed that the centrally mediated effects of morphine on the immune response of laboratory rats is markedly enhanced by psychological stress. Other studies are examining the morphine-induced conditioning of the immune system. Enkephalins, which are endogenous opioids considered to be possible neurotransmitters, appear to be important regulators of immune responses. For example, studies show that by regulating white blood cells in a developing fetus, enkephalins may have a role in the development of immune function in the maturation of fetal tissues and organs. This information could have significance for further research into the progression of HIV disease in infants and children.

These opioid agonists (opiates and other compounds that stimulate opioid responses) characteristically suppress immune responses. On the other hand, opioid antagonists, compounds that block the opioid response, also block most immune-suppressing actions of opioid agonists. NIDA-funded basic researchers have observed this blocking of the suppressing action by naloxone, one of the family of opioid antagonists used to treat heroin overdoses. These findings support the view that opioid agonists suppress immune responses by employing typical opiate mechanisms and present important ramifications for further studies of immune function and disease.

In a study of rhesus monkeys infected with simian immunodeficiency virus (SIV), an animal model for studies of HIV and AIDS, NIDA-supported researchers have shown that opioids increase the mutation of the virus in the early stages of SIV infection. These results suggest that, in humans, this type of mutation could lead to the development of a form of the virus that is resistant to zidovudine, or AZT, the drug most commonly used to treat AIDS patients.

Evidence from other studies indicates that cannabinoids, the psychoactive components of marijuana, also suppress the immune response. NIDA-funded researchers are investigating how this process differs from immune system actions mediated by the central nervous system (CNS), how the immune cells differ from those in the CNS, and how certain cannabinoid-like compounds that occur naturally in the body act on these different systems. Other scientists have determined that one cannabinoid (THC) interferes with the ability of immune cells to target and destroy cancer cells as well as invading bacteria, fungi, and viruses.

Still other NIDA-funded basic research is examining how the abuse of nitrite inhalants depresses the immune response, thus apparently increasing abusers' risk of acquiring AIDS. The effects of abuse of anabolic steroids on the immune system are also being studied.

Clinical Research

NIDA's Division of Clinical and Services Research supports clinical studies of HIV and AIDS among drug users, including people in and out of drug abuse treatment. NIDA's multidisciplinary research program involves studies of behavioral and biological factors associated with drug abuse and HIV infection. Current studies of HIV focus on HIV disease progression, treatment of HIV-infected drug users, linkage of drug abuse treatment and primary medical care, the relationship between HIV and other infectious diseases common among drug users, and studies of HIV disease in pregnant women and their infants. The goal of the clinical research program is to understand the unique aspects of HIV and AIDS among drug users to develop better prevention and treatment strategies.

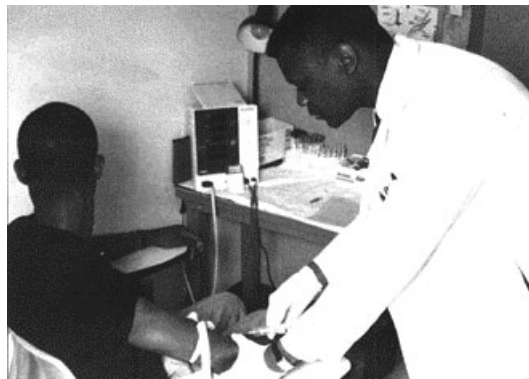
For nearly 10 years, NIDA has supported a program of longitudinal research on the natural history and progression of HIV disease in drug users. Long-term studies provide data on both the incidence and prevalence of HIV disease in various groups of drug users and permit researchers to define the clinical course of the disease from early infection through its long-term consequences. These studies require medical assessment and followup of complex conditions while also evaluating the impact of behavioral and medical interventions on the course of the disease.

Because drug users have poor access to medical care in general as well as to HIV-specific treatment, and because adherence to treatment regimens is often a problem,

AIDS-related health services research—including delivery of treatment, linkage of drug abuse treatment and primary care, and access and adherence to medication protocols—is a component of NIDA's clinical research program. Other areas of focus include barriers to medical treatment; psychosocial and behavioral factors associated with success or failure of treatment regimens; the impact of episodic or erratic patterns of drug use on treatment effectiveness; fetal and infant outcomes; and how HIV disease medications, HIV-related opportunistic infections, and other diseases prevalent among drug users affect HIV progression and the long-term survival of the victim.

Development of better treatment strategies for HIV-infected pregnant women is a high priority, given the recent findings that use of AZT can significantly reduce the rate of mother-to-infant HIV transmission.

Opportunities exist for enhanced studies of effective treatment for drug-using women in collaboration with large national clinical studies supported by the National Institutes of Health. For example, through a collaborative agreement with the National Institute of Allergy and Infectious Diseases at NIH, NIDA supports followup studies of a group of pregnant HIV-infected women in New York City, most of whom are drug users. Research on the role of active drug use in maternal-infant HIV transmission and the effectiveness of AZT treatment in preventing such transmission is a focus of this effort.



AIDS-related health services research is a component of NIDA's Clinical Research Program.

Suppression of the immune system, characteristic of HIV, puts infected individuals at higher risk for other infectious diseases, including tuberculosis. NIDA is supporting a program of research on TB, one of several infections common among drug users. The focus of this research includes studies of the consequences of coinfection with HIV and TB, as well as the development of better strategies to screen for TB among drug users and to improve access and adherence to treatment. Treatment regimen adherence is critical in controlling further transmission of TB and in preventing the development of treatment-resistant strains of TB.

Other current areas of HIV clinical research include studies of markers and predictors related to the virus and the immune system that are associated with rates of disease progression and survival, hepatitis C virus infection among HIV-infected and uninfected active drug users and the impact on HIV disease course, the interaction of components of the immune system with the virus and the impact on disease status and progression among

HIV-infected children, determination of viral strain differences that may influence the rate of disease progression, and the impact of ongoing drug injection on the activation of the immune system and the proliferation of viral strains.

For nearly 10 years, NIDA has supported longitudinal research on the natural history and progression of HIV disease in drug users.

NIDA-funded clinical research has contributed substantially to current knowledge about HIV infection and disease progression in populations of drug users. For example:

- Although basic research indicates that opioids can modulate (suppress or enhance) the immune response, clinical studies of HIV disease progression, as measured by decline in immune cell (CD4) counts, have not demonstrated that immune suppression is more rapid among actively injecting polydrug (cocaine and heroin) users than among other risk groups.
- Studies of clinical manifestations and predictors of HIV disease progression among drug users found that progression to AIDS was best predicted by low numbers of immune (CD4) cells; the presence of an oral infection called candidiasis; bacterial infections including sepsis, pneumonia, and TB; and by nonuse of AZT.
- Smoking of illicit drugs increases the risk of contracting bacterial pneumonia among HIV-infected injecting drug users who have a history of AIDS-related pneumonia.
- HIV infection appears to be associated with increased rates of endocarditis infection, a serious heart disorder common among injecting drug users, but the frequency of injection apparently is not a factor.
- Although results of a skin test indicating immune suppression when testing for TB infection in HIV-infected patients have been used as a reason to initiate TB therapy, recent clinical studies of injecting drug users show that the skin-test responsiveness can fluctuate over time, bringing into question its reliability for use in determining treatment initiation.
- New HIV infection rates among HIV-negative drug users who remained continuously in methadone treatment for 18 months were found to be six times lower than the incidence rates in comparable drug users who remained out of methadone treatment for the same time period.
- Studies of several laboratory markers indicative of immune status and duration of HIV infection and the relationship of these markers to the risk of developing HIV disease indicated that only low immune cell (CD4) counts were independently related to increased risk of AIDS, that CD4 counts of less than 150 were strongly related to immediate risk of adverse outcome, and that disease outcomes tended to occur as a progressive series of events (constitutional symptoms, oral candidiasis, bacterial infections, and AIDS). **NN**

AIDS Brings Greater Research Obligation, More Potential for Results

By NIDA Director Alan I. Leshner, Ph.D.

In 1994, the Centers for Disease Control and Prevention (CDC) received 80,691 new reports of Americans with AIDS. This 1-year toll is almost one-fifth of all U.S. AIDS cases ever reported.

While the epidemic continues its spread, it is also evolving, targeting different population groups. We have clear evidence that drug-related transmission of HIV, the AIDS virus, is increasing significantly. Analysis of new CDC data suggests a majority of new HIV cases last year involved drug abusers—heroin and crack addicts—and their sexual partners. While new cases among homosexual and bisexual men are decreasing, heterosexual transmission of HIV is increasing. In fact, the fastest-growing subgroup of patients with AIDS over the last several years has been heterosexual men and women, most of whom are linked sexually to drug users.

The changing nature of the AIDS epidemic, especially its growing association with drug abuse, increases the Institute's responsibilities in fulfilling its public health mission. When you consider how closely drug abuse is linked to the spread of AIDS, it should be no surprise that NIDA allocates one-third of its budget to AIDS-related aspects of drug abuse.

NIDA has supported and will continue to support research aimed at developing strategies to reduce drug abuse as an important contribution to AIDS prevention efforts. NIDA-supported researchers have shown that drug abuse treatment and street outreach to drug abusers not in treatment can be effective in changing high-risk sexual and drug-use behaviors associated with contracting and transmitting HIV. Scientists have shown that it is possible to get addicts to change these high-risk behaviors even while they are still using drugs.

Over the years, NIDA-funded researchers have also probed drug-related aspects of AIDS in the areas of epidemiology, disease origin and progression, immunology, and neurobiology. They have shed new light on treatment, interactions between disease medications and those for

drug abuse, health care services delivery, and transmission of HIV from mothers to their infants.

While some NIDA-funded researchers have been learning how to teach street addicts to modify high-risk drug-related behaviors, other investigators have been conducting cellular and molecular studies of the connections between drugs of abuse and the body's disease-fighting immune system.



Beyond research in the streets and the laboratories, NIDA has supported research training programs to increase the ranks of researchers qualified to deal with the scientific and medical aspects of AIDS. In past years, NIDA provided training in AIDS and related drug abuse issues to thousands of treatment counselors and administrators and helped 35 States develop training programs on AIDS and drug abuse. In addition, the Institute has mounted a number of informational and public education initiatives

to warn people about the links between drug abuse and AIDS. These initiatives have included, for example, nationwide TV campaigns aimed at young people.

NIDA is committed to building on its previous research. That means the Institute is calling on researchers, in turn, to expand their horizons in designing future investigations, to consider AIDS- and HIV-related issues in the design of new experiments. We encourage scientists to develop and submit their own investigator-originated funding requests for drug-abuse-related AIDS research.

Some 14 years into the AIDS epidemic, NIDA is still broadening the scope of its AIDS research, building on progress. We must learn more about how to improve drug abuse treatment and outreach programs to reduce high-risk behaviors associated with drug use and sexual practices, how to prevent relapses to high-risk behaviors, and how to improve clinical management of HIV-positive drug abusers. We must develop more research-based responses to the special AIDS risks and needs of minorities, women, infants, and children. We must probe the enigmatic connection between drugs of abuse and the

immune system. And we must ensure that HIV risk-reduction strategies are incorporated into all appropriate NIDA-funded research strategies.

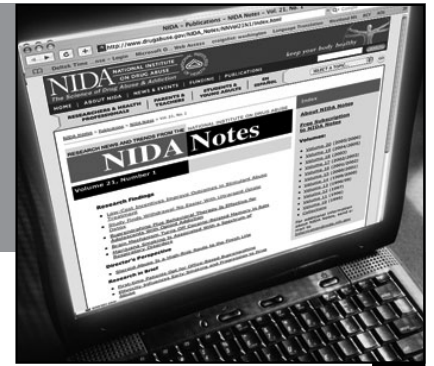
In short, we must further demonstrate to the public that preventing the spread of AIDS means, in large part, preventing drug abuse.

In broadening the scope of our research, we are not lessening our commitment to drug abuse research. By mounting an enhanced, research-based response to the AIDS epidemic, NIDA is also tapping new opportunities for scientific advancement that extend beyond AIDS. The

Institute's AIDS research helps us learn more about how drugs of abuse work in the central nervous system, how disease spreads among at-risk subgroups of drug abusers, how drug-related cellular and molecular mechanisms modulate the progress of disease, and how the immune system functions to protect the human body from invading microorganisms.

NIDA's broadened research agenda will help us learn how to devise innovative therapies and responses effective not only against AIDS but also against drug abuse. **NN**

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