A Collection of

NIDA NOTES

NATIONAL INSTITUTE ON DRUG ABUSE

30 Years 1974-2004

Articles That Address

Drugs and Aids

U.S. Department of Health and Human Services
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Table of Contents

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 19, Number 1 (April 2004)

NIDA at 30: Committed to Scientific Solutions for Drug Addiction Problems

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

This year, NIDA celebrates 30 years of scientific inquiry marked by tremendous strides in advancing the frontiers of drug abuse research and reducing the suffering, community disruption, and public health costs of drug addiction. In 1974, NIDA was a small institute striving to develop an effective Federal response to a critical public health crisis—burgeoning drug abuse in the United States. Today, the Institute is the world's foremost source of scientific knowledge on the prevention and treatment of the chronic, relapsing brain disorder of drug addiction.

In its first decade, NIDA established national data-collection systems to increase understanding of the nature and extent of drug abuse. In addition to developing a nationwide network of treatment, prevention, and clinical and research training programs, the Institute also initiated a basic science research program that produced groundbreaking discoveries on the brain and its molecular and neurochemical methods of communication. Today, scientists draw on these discoveries to create new medications to treat drug abuse and other mental disorders.

In 1981, a congressional mandate shifted NIDA's primary mission to expanding the borders of scientific knowledge about drug addiction and ensuring that this knowledge be used to prevent and treat the disease. Throughout the 1980s, NIDA-supported researchers mined information on the causes, correlates, and consequences of drug abuse and addiction and generated a range of prevention and treatment approaches for heroin, marijuana, and nicotine abuse and the new threat of crack cocaine. As a result, practitioners today have highly effective opiate and nicotine treatment medications, a range of behavioral treatments for cocaine abuse, and the underlying principles of successful prevention and treatment to use in reducing drug abuse.

In 1986, the Nation once again turned to NIDA, this time for help in addressing the emerging AIDS epidemic. Within a year, NIDA nearly tripled its research on AIDS and drug abuse to address the major role injection drug use plays in transmitting HIV, the virus that causes AIDS. The Institute's massive effort rapidly established AIDS outreach projects around the country, educated out-of-treatment drug users and their sex partners on ways to prevent HIV transmission, and proved that these approaches could reduce the risky drug use and sexual behaviors that were fueling the spread of HIV/AIDS. This body of AIDS research, bolstered by an additional decade of AIDS discoveries, informs the NIDA-promulgated principles of HIV prevention among drug users that now curb the spread of HIV/AIDS.

In 1992, Congress affirmed the importance of NIDA's research to the Nation's public health when it made NIDA part of the National Institutes of Health, the world's premier biomedical research agency. During the ensuing decade, NIDA mounted major new research and communications programs to counter alarming increases in young people's use of methamphetamine, heroin, and "club drugs," such as ecstasy (MDMA). The Institute's basic and clinical research programs applied revolutionary new techniques in molecular biology and brain imaging technologies to rapidly advance understanding of the underlying neurobiological and behavioral processes that increase vulnerability to drug abuse, foster the transition to addiction, and prevent many patients from achieving successful treatment results. At the same time, NIDA launched new initiatives to close the gap between research and practice. As a result, drug abuse scientists and practitioners now are collaborating to improve drug abuse prevention and treatment research and services in communities across America.

With its outriders of mental illness, HIV/AIDS, and hepatitis C; its public health and criminal justice costs; and its devastation of homes and neighborhoods, drug addiction continues to demand a comprehensive research program focused on these problems. NIDA has assembled such a program and remains committed to its purpose—the alleviation of suffering through scientific advance. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 19, Number 1 (April 2004)

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 preceeding 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.

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.

"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 childcare, 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 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.

Sources

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- Sterk, C.E.; Theall, K.P.; Elifson, K.W.; and Kidder, D. HIV risk reduction among African-American women who inject drugs: A randomized controlled trial. *AIDS and Behavior* 7(1):73–86, 2003. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 17, Number 2 (May 2002)

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.

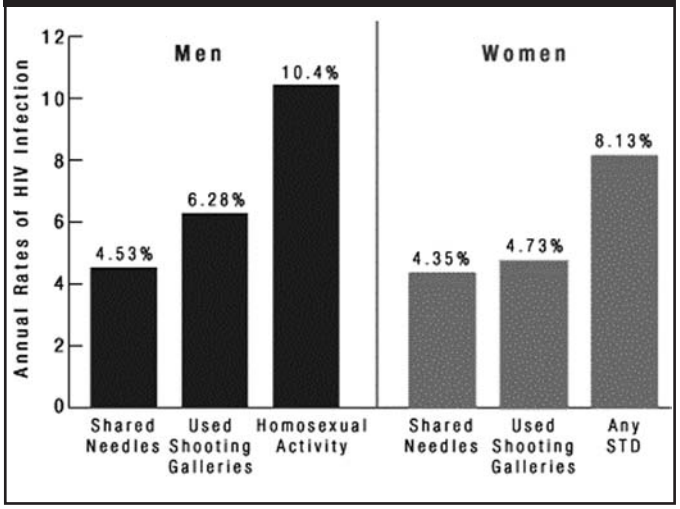
"In the past, we assumed that IDUs who were HIV-positive had been infected with the virus through needle-sharing," says Dr. Steffanie Strathdee of the Johns Hopkins University Bloomberg School of Public Health in Baltimore, who conducted the NIDA-funded study. "Our analysis indicates that sexual behaviors, 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

High-Risk Sexual Behavior Leading Cause of HIV Infection Among Injection Drug Users in 10-Year Study



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.

they had used shooting galleries had an HIV incidence 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." NN

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.

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Research Findings

Volume 17, Number 1 (April 2002)

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 NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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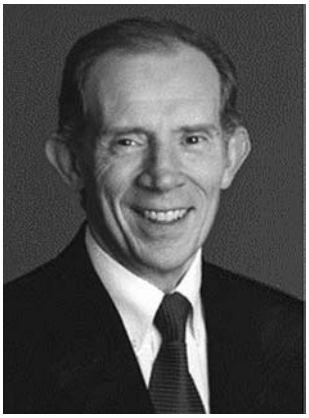
NIDA Research Advances Global Efforts To Prevent and Treat AIDS

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.

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

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 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."

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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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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.

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.

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 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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 17, Number 1, (April 2002)

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.

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 16, Number 6 (February 2002)

Special Interest Groups Focus CTN's Research

NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) provides a unique opportunity for researchers and practitioners to work together to test research concepts that can help them fill gaps in knowledge about drug addiction treatment. To better focus future research on specific treatment areas and the needs of different populations, participants who share an interest in a common treatment issue have formed six special interest groups, and two more are in the works. The groups address research and treatment interests in the following areas:

- HIV/AIDS
- Adolescent treatment
- Women and gender issues
- Comorbid patients
- Court-involved patients
- Ethnic minority populations
- Behavioral therapy (planned)
- Pharmacotherapy (planned)

The groups meet regularly and serve as expert resources for the CTN in their respective areas, says Dr. Betty Tai, who directs NIDA's CTN office. They fulfill such functions as assessing current practice in their special areas, identifying promising research-based interventions, developing new research concepts for testing, and preparing long-range research plans. For example, the first group to form—the HIV/AIDS group—has developed an AIDS research strategy for the CTN and proposed treatment research concepts for HIV prevention and treatment in drug treatment settings for protocol development.

Seminars held at the CTN's annual meeting reflected the input of these special interest groups and illustrated how they are broadening the scope of the CTN's treatment research agenda. The seminars covered challenges in the treatment of substance abuse disorders among adolescents using family therapy and treatment medications, treatment issues for men and women substance abusers with trauma histories and post-traumatic stress disorder, issues in the assessment and treatment of substance abusing patients with coexisting mental disorders such as antisocial personality disorder and depression, and the impact of HIV/AIDS and HIV interventions on substance abuse treatment in CTPs. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 16, Number 3 (August 2001)

Drug Injectors Sharing Cookers and Cotton Increase Their Risk of Hepatitis C

By Josephine Thomas, *NIDA NOTES* Contributing Writer

The hepatitis C virus (HCV) is extremely common among injection drug users (IDUs); some regions of the United States have reported prevalence rates as high as 90 percent in their IDU populations. Previous research has shown that sharing contaminated needles is responsible for many of these infections. NIDA research now has shown that IDUs can contract hepatitis C not only from sharing needles, but also through sharing other drug injection equipment, especially cookers and filtration cotton.

The research team, led by Dr. Holly Hagan of the Seattle-King County Public Health Depatment, evaluated risk factors for HCV by analyzing data from their Risk Activity Variables, Epidemiology and Networks (RAVEN) study. The RAVEN study collected information and blood samples between June 1994 and May 1997 from 2,879 IDUs in Seattle area programs that provided them with clean needles in exchange for used ones.

"As needle sharing declined throughout the 1980s and 1990s," says Dr. Hagan, "it became possible to consider other risk factors for the transmission of blood-borne diseases among IDUs. This was one of the principal goals of the RAVEN study. We knew that the IDUs who participated in that study were less likely to share needles after they received counseling, but that sharing of drug cookers and filtration cotton was commonplace."

Of the initial 2,879 IDUs, only 507 (17.6 percent) tested negative for HCV at the conclusion of the RAVEN study. After a year, researchers were able to collect blood samples and administer a questionnaire to 317 of these 507 participants. Of these, 259 reported having injected drugs during the followup period, and of this group, 53 (16 percent) had become HCV-positive during the 1-year followup period. The questionnaire also asked participants if they had shared needles at any time during the previous year and if they shared cookers and cotton.

Syringe sharing was associated with a three-fold higher risk of HCV infection as opposed to IDUs who did not share syringes, according to Dr. Hagan. Among the much smaller group that did not share syringes, "The risk of HCV infection was also three-fold higher among those who did not share syringes but did share a cooker and cotton." Dr. Hagan notes that the study's ability to evaluate the risk of sharing equipment other than syringes was reduced by the limited number of HCV-negative IDUs who did not share syringes but who did test positive over the course of the study. This group numbered only 11 out of the 53 who became positive over the course of the study.

With respect to frequency of sharing equipment, the study confirmed the link between more syringe sharing and higher risk of HCV—the rate of infection was relatively higher among those who reported sharing syringes sometimes, usually, or always than among those who reported rare syringe sharing. However, the risk elevation associated with cookers and cotton appeared to be the same for individuals who shared this equipment regardless of the frequency of sharing."

"Prevention education has been successful in a large portion of the IDU population, but over time, some high-risk groups will become more identifiable," says Dr. Peter Hartsock of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse. "This research should lead to the development of interventions that will have a greater impact than previous interventions on populations at risk of developing HCV and other blood-borne diseases. With this new data, we can better adjust interventions and programming to meet the needs of these populations," he says. Dr. Hagan notes that Seattle-King County Public Health Department staff have already revised their prevention messages to include the risks of

Hepatitis C Is America's Most Common Blood-Borne Infection

Approximately 36,000 new cases of acute hepatitis C infection are reported each year in the United States, according to the Centers for Disease Control and Prevention (CDC). The number of Americans with chronic hepatitis is unknown—although CDC estimates the number at 4 million—because the symptoms of the disease can be minimal. In chronic hepatitis C, progressive injury to liver cells over 2 to 4 decades often leads to cirrhosis of the liver and liver cancer. Hepatitis C-related liver failure is now the leading indication for liver transplants in the United States. The disease also is the leading cause of liver cancer and is responsible for 8,000 to 10,000 deaths a year in this country.

sharing equipment such as cookers and cotton, as well as sharing needles, but adds that many IDUs are not yet aware that these are high-risk practices.

"I think it will be increasingly feasible to study each step of the injection process in terms of blood-borne viral transmission," Dr. Hagan says. "Once we understand the powerful risk factors, such as sharing needles and equipment, it will be possible to move on to other factors that perhaps do not carry as strong a risk but nonetheless are responsible for a significant number of infections. Studies to measure the risk of transmission through less common routes of exposure are important because they enable us to extrapolate general epidemiologic information that will have direct implications for the prevention of all types of blood-borne viruses in the population as a whole."

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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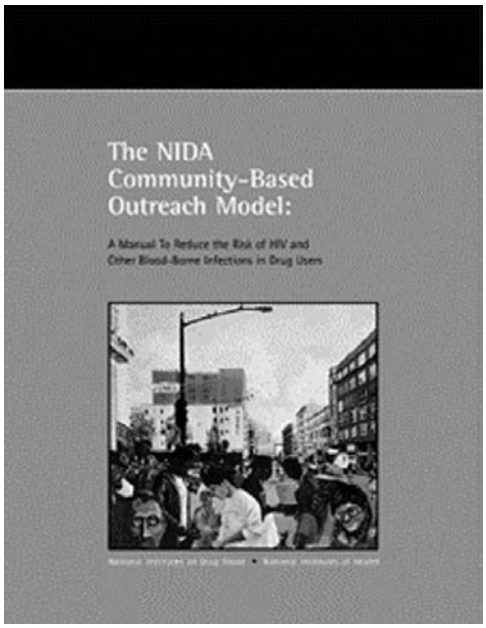
Preventing Drug Abuse-Related Infectious Diseases Through Community Outreach

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.

Copies of the manual, including cue cards, can be obtained free from the National Clearinghouse for Alcohol and Drug Information, 1-800-729-6686 or 1-800-487-4889 (TDD); fax requests to 1-301-468-6433. Ask for publication number BKD366. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 6 (January 2001)

International Conferences Focus On NIDA's HIV/AIDS Research

By Patrick Zickler, *NIDA NOTES* Staff Writer

NIDA's research into the relationship between drug abuse and HIV/AIDS served as a focal point for two international meetings that preceded the 13th International AIDS Meeting in Durban, South Africa. NIDA—in partnership with the Center for Drug Abuse Research at Howard University in Washington, DC, the Medical Research Council of South Africa, and other United States and South African agencies—cosponsored a conference held in Cape Town, South Africa, between July 1 and 5 on the topic "Substance Abuse, Crime, Violence, and HIV/AIDS as Consequences of Poverty: Strategies for Prevention, Intervention, and Treatment in the U.S. and South Africa." The conference brought together researchers from the U.S. and South Africa, who discussed mechanisms for building a broader research infrastructure and capacity in South Africa, as well as development and expansion of partnerships for research into the interrelationship of drug abuse, HIV/AIDS, and infectious diseases such as hepatitis and tuberculosis among populations living in poverty.

NIDA Director Dr. Alan I. Leshner delivered a keynote address at the conference. In addition, Dr. Leslie Cooper, Dr. Dionne Jones, and Mr. Arnold Mills made presentations at the conference. These NIDA staff members, along with Dr. Lula Beatty, also served on the conference planning committee and acted as facilitators in conference work groups. In the work groups, participants identified ways to expand and coordinate networking mechanisms and other collaborative efforts between researchers in South Africa and the U.S., initiated development of concept papers outlining areas in which additional research might be most productive, and identified best practices for prevention and early intervention being used in each country so that research gains can be shared while remaining sensitive to cultural differences.

The Third Annual Global Research Network (GRN) Meeting on HIV Prevention in Drug-Using Populations, cosponsored by NIDA and a consortium of international organizations, was held in Durban, South Africa, July 5 through 7. NIDA was instrumental in the creation of the GRN, which focuses on the dissemination and application of research-based strategies for prevention of HIV infection among drug users.

Among those discussing drug abuse at the Cape Town conference were (standing from left): O. Jackson Cole, senior associate provost, Howard University; Priscilla Reddy and Neo Morojele, South African Medical Research Council; Alfred Tsetsane and Andrew Aphane, Department of Correctional Services of South Africa; Anne Gloria Moleko, University of Pretoria/South African Alliance for Prevention of Substance Abuse; Jean Oyemade Bailey, Center for Drug Abuse Research, Howard University; Ronald Braithwaite, NIDA-funded researcher, Emory University; (seated from left) Ben Skosana, M.P., Minister of Correctional Services of South Africa; and Steve Tshwete, M.P., Minister of Safety and Security of South Africa

"Our goal is to advance the scientific exchange of empirically based research data on HIV prevention strategies for drug-using populations so that HIV prevention researchers and community providers can develop and implement effective interventions," Dr. Leshner said in a keynote address.

Dr. Henry Francis, Ms. Helen Cesari, and Ms. Elizabeth Lambert of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse served on the GRN meeting's planning committee. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 4 (September 2000)

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 or from the National Clearinghouse for Alcohol and Drug Information (NCADI), P.O. Box 2345, Rockville, MD 20847-2345, (800) 729-6686. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 4 (September 2000)

NIDA Supports Research on Ethical Issues in Drug Abuse and HIV/AIDS Studies

By Robert Mathias, *NIDA NOTES* Staff Writer

NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) is encouraging research applicants in the area of drug abuse and HIV/AIDS to respond to a recent NIH-wide Program Announcement that calls for research focusing on ethical considerations in human studies.

The religious, cultural, and family values surrounding drug abuse and HIV/AIDS are important influences in clinical and research decisionmaking for both patients and providers. Yet, few studies have examined how best to provide information about study methods and procedures to participants, the effects of different recruitment strategies on retention of study participants, or the effects of investigator characteristics and behavior on levels of study recruitment, retention, and withdrawal.

The Program Announcement, "Research on Ethical Issues in Human Studies" (PA-99-079), is sponsored jointly by the National Institutes of Health and the Centers for Disease Control and Prevention. CAMCODA seeks to stimulate studies, in addition to investigator-initiated projects, that focus on participant or research process issues. Possible research topics include:

- evaluation of the cognitive ability required for patients to comprehend and consent to experimental procedures and risks;
- how potential research participants weigh risks and benefits;
- ways to address special issues related to research and medical records;
- disparate health needs among special populations;
- ethical issues surrounding the HIV/AIDS pandemic and its relationship to drug abuse; and
- the challenges in ethical design and conduct of cross-cultural studies, especially in research carried out in low- and middle-income areas.

Application deadlines are September 1, January 2, and May 1. Potential applicants can obtain more information on targeted ethics studies by contacting CAMCODA's Noble Jones or J.C. Comolli at 301-443-1801. Current research Program Announcements are available on NIDA's home page at www.drugabuse.gov under Funding Information. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 4 (September 2000)

Conference Focuses on Linked Issues of Drug Abuse, HIV, and Hepatitis C

By Josephine Thomas, *NIDA NOTES* Contributing Writer

The intricate relationships between the epidemics of drug abuse, HIV/AIDS, and hepatitis C were the focus of discussion at "Drug Use, HIV, and Hepatitis: Bringing It All Together," a conference sponsored jointly by NIDA, the Center for Substance Abuse Treatment (CSAT), and the Centers for Disease Control and Prevention (CDC) held in Baltimore in May.

"The connection between drug abuse and HIV has been recognized for some time," said NIDA Director Dr. Alan I. Leshner. "It's unfortunate that it has taken us this long to take on hepatitis C as a related issue, because the reality is that these three diseases are intertwined." Dr. Leshner emphasized that a logical approach to preventing the spread of HIV and hepatitis C is treatment for drug addiction.

NIDA Director Dr. Alan I. Leshner and CSAT Director Dr. Westley Clark at the conference. (Photo courtesy of Danya International, Inc.)

Like HIV, the hepatitis C virus (HCV) is spread through contact with an infected individual's blood and—although this is less common than with HIV—through sexual contact. According to CDC, approximately 4 million Americans have been infected with HCV, of whom 2.7 million are experiencing chronic symptoms. At least 60 percent of the estimated 36,000 individuals infected each year will contract the disease through the use of contaminated injection drug equipment. Eight thousand to 10,000 Americans are expected to die of HCV-related liver disease this year.

At workshops during the conference, scientists from NIDA and CDC discussed ways to prevent the spread of HCV, as well as ways to assess and treat patients with both HCV and HIV. Attendees participated in skills building workshops that were led by NIDA researchers and other experts and that focused on topics such as the problem of HCV in the prison system; the role of microbicides in prevention; prevention strategies for high-risk populations; the epidemiology of HIV and hepatitis infections among young adults and recently initiated injection drug users; prevention of opportunistic infections; improving adherence to prevention and treatment strategies; integrating treatment into public health settings; methods for conducting patient needs assessments; drug interactions; integrating mental health care into comprehensive treatment planning; and more.

At a press conference held during the meeting, Dr. Leshner announced the release of NIDA's new Community Drug Alert Bulletin on Hepatitis C and also announced that NIDA is publishing the first science-based guide for HIV outreach, entitled *The NIDA Community-Based Outreach Model: A Manual to Reduce the Risk of HIV and Other Blood-Borne Infections in Drug Users.*

Dr. Leshner noted that NIDA, CSAT, and CDC all are working with the scientific community, substance abuse treatment programs, and the HIV community to increase knowledge of these diseases among people at risk and the general public. "Substance abuse prevention and treatment practitioners are on the front lines of preventing and treating HIV, HCV, and other sexually transmitted diseases (STDs), but need to focus on the whole problem—not just one aspect of it," added Dr. Westley Clark, director of CSAT. This means developing and implementing comprehensive approaches that integrate ways to reduce the risk of contracting and spreading these diseases, he noted.

Dr. Leshner noted that although drug abuse and addiction affect everyone in the United States either directly or indirectly, most people deal with the issue based on their individual ideologies and cultural myths. "Advances in science have fundamentally revolutionized the way we look at the brain and at drug addiction as a brain disease," he said. "We now know that drug abuse is a preventable behavior, but addiction is a disease." Treatment is essential because "drug abuse is a major vector for transmission of other diseases, including HIV, HCV and other types of hepatitis, other STDs, and tuberculosis." The challenge not only will be getting drug-abusing and drug-addicted individuals into treatment, but also will be getting those who have

not yet entered treatment to change their behaviors, he said.

"We now have the science base we need to understand how these diseases work alone and together, and this must be the foundation of our work," Dr. Leshner said. "What we have learned through the scientific study of the brain helps explain why most addicts can't just stop taking drugs. But this does not mean that they cannot reduce their risk behaviors for related diseases."

Dr. Henry Francis, director of NIDA's Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA), emphasized to participants that drug abusers tend to be as willing to participate in treatment as anyone else if they have regular contact with a primary care doctor. "CAMCODA's goal is to expand NIDA's treatment portfolio from a focus on how the disease and infection process works to a focus on why and how people are exposed to risk and what is needed to treat and prevent the disease," he said. Because HCV is a significant problem in the drug-injecting population, treatment provided to individuals who have both HIV and HCV must be carefully planned and monitored. Interferon—the standard treatment for HCV—can cause mood disorders and other symptoms that may encourage drug abuse or interfere with treatment for HIV. Drug use should not be considered a contraindication for treatment of either HIV or HCV, he said.

In panel discussions, experts from CDC's Division of HIV/AIDS Prevention told conference participants that HIV infection rates among injection drug users remain high and that Hispanics and African Americans are disproportionately affected by the disease. Since 1992, death rates among AIDS-infected persons have declined dramatically due to the introduction of highly effective antiretroviral medications. However, the infection rate for hepatitis C in this population has risen as the number of deaths from HIV has declined. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 3 (August 2000)

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 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.

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.

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."

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 15, Number 1 (March 2000)

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.

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-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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 6 (March 2000)

NIDA Symposium Spotlights 25 Years of Drug Abuse Research

By Robert Mathias and Patrick Zickler, *NIDA NOTES* Staff Writers, and
Barbara Shine and Raymond Varisco, Contributing Writers

In these pages we present a sampling of the presentations made by speakers whose work has helped NIDA uncover the biological and behavioral structure of drug abuse and develop, test, and implement new treatments and prevention programs.

In the future, effective drug abuse treatment will continue to require a combination of medications and behavioral interventions, said Dr. Herbert Kleber of the Columbia University College of Physicians and Surgeons in New York City. He noted that past research has produced medications, such as methadone and LAAM, that can treat opiate addiction effectively, as well as successful behavioral drug abuse treatments that include relapse prevention and motivational strategies. However, he said, 75 percent of heroin addicts are not in treatment, and existing medications all have some drawbacks. Therefore, we need both better medications and better ways to get patients into treatment for heroin addiction.

NIDA's year-long celebration of the Institute's 25-year history of research culminated on September 29 with a symposium at the National Institutes of Health in Bethesda, Maryland. The event highlighted NIDA's past and present accomplishments and offered a look at the direction and scope of future research.

Medications developed for conditions such as depression and epilepsy will continue to be a source of new addiction treatment medications, and new compounds will target specific brain mechanisms involved in drug abuse, Dr. Kleber predicted. Research to develop such compounds—especially compounds aimed at cocaine, for which there is no generally effective medication—will need to focus on the complex actions of drugs on multiple neurotransmitters in the brain, he said. The next few decades should see the development of vaccines that block the effects of drugs such as cocaine and PCP and medications with less toxicity and abuse potential than current ones, Dr. Kleber said.

In the past, drug abuse prevention efforts focused on increasing the public's knowledge about the dangers of drug abuse. Today, research-based prevention approaches

Dr. Mary Ann Pentz discusses community-based drug abuse prevention programs.

focus on counteracting the personal, social, and environmental factors that influence children and adolescents to use drugs, according to Dr. Mary Ann Pentz of the University of Southern California in Los Angeles. "Community-based prevention programs must have multiple components, involve all segments of the community, encompass different settings, and administer periodic booster sessions to effectively address multiple risk factors and reinforce community-wide norms against drug use," she said.

Implementing broad-based community programs takes time, Dr. Pentz noted. For example, it took 5 years of working with various community segments to implement effective programs in Kansas City, Missouri, and

Dr. Herbert Kleber tells symposium participants that effective drug abuse treatment will include both medications and behavioral interventions.

Indianapolis, Indiana, but followup research indicates that the effort paid off in long-term reductions in drug use and other problem behaviors among children and adolescents.

"If all 11-year-old children in the U.S. participated in a similar prevention program, it would save $5.6 billion in alcohol- and drug-abuse-related costs by the time those children reach age 25," Dr. Pentz estimated.

Since the onset of the AIDS epidemic in the mid-1980s, drug abuse research has made many contributions to preventing AIDS and increasing understanding of how the disease progresses, said Dr. David Vlahov of the New York Academy of Medicine in New York City. Dr. Vlahov noted that studies have shown that a variety of drug abuse practices—such as sharing syringes, frequent injection, and injecting drugs in "shooting galleries"—are key risk factors for transmitting HIV. Recent research indicates the risk of becoming infected with HIV is particularly high when drug users first begin to inject drugs. "This finding underscores the importance of early targeted prevention efforts," Dr. Vlahov said. A comprehensive prevention approach that includes drug abuse treatment; HIV testing, counseling, and education; outreach to drug users not in treatment; behavioral strategies; and needle exchange is effective in reducing the spread of HIV, Dr. Vlahov said.

"NIDA's solid scientific research effort serves as a basis for community and school-based programs that work in preventing drug abuse generally and, more important, in preventing drug abuse among the Nation's youth."

Director of the White House
Office of National Drug Control Policy
General Barry McCaffrey

The development of potent anti-viral medications in recent years has made possible a new strategy to prevent transmission of HIV by injecting drug users (IDUs) who are already infected, Dr. Vlahov said. "We want to get more IDUs into therapy and maximize their adherence," he said. "Research shows that these medications can significantly reduce viral load in drug users, dramatically lowering the risk of transmitting the disease." Additional efforts are needed to increase HIV-positive IDUs' access to these medications, achieve strict adherence to rigorous medication regimens, assess whether injecting drugs increases HIV's resistance to the medications, and evaluate interactions between anti-HIV medications and drug abuse treatment medications, he said.

Dr. Huda Akil, of the University of Michigan in Ann Arbor, focused on the neurobiology of stress and depression and the biology of endorphins and other molecules related to substance abuse. Dr. Akil described results of NIDA-supported research into the effects of stress on

"NIDA was established to bring the power of science to bear on the Nation's drug abuse problems, and the first 25 years of this crucial investigation have produced groundbreaking discoveries about the nature of drug abuse. We have established the reality that drug abuse is not a moral flaw or a simple behavioral problem. It is a brain disease with biological causes and consequences as well as profound and complex social and behavioral components."

NIDA Director, Dr. Alan I. Leshner

drug-taking behavior and the neurobiological basis of individual differences in this interaction. "A research approach that attempts to understand the biological bases of emotional behavior will expand our understanding of the role of emotion in drug abuse as well as other areas of health and illness," Dr. Akil said.

Dr. Hans Breiter, a NIDA-supported researcher at the Massachusetts General Hospital in Boston, described the role of brain imaging techniques in drug addiction research. The development of new pharmacological treatments for drug abuse will rely on imaging techniques to illuminate specific brain mechanisms, Dr. Breiter said. The techniques allow researchers to identify the specific brain regions affected by drugs, an important preliminary step in the development of agents that can repair a brain changed by chronic drug use.

Dr. Floyd Bloom, editor-in-chief of Science magazine and chairman of the department of neuropharmacology at The Scripps Research Institute in La Jolla, California, noted that NIDA's history has been marked by surprising discoveries that shape and focus drug abuse research. "The discovery and description of the molecular structure of opiate receptors in the brain was a momentous milestone in science," Dr. Bloom said. "We now know that receptor sites are only a small part of 'reward circuits' that play crucial roles not only in drug abuse but in hunger, thirst, and pleasure. There is still much we don't know," he said.

"What specific molecular events in cells and circuits throw the 'switch' that results in a transition from drug use to abuse and dependence? What conditions predispose some individuals to vulnerability to drugs?" The answers, Dr. Bloom told the audience, will be found by continuing NIDA's 25-year history of neuroscience research.

Dr. Jose Szapocznik, director of the Center for Family Studies at the University of Miami, described the influences that lead to adolescent drug use and summarized key components of successful prevention programs.

"Parents' involvement in the lives of their children is by far the strongest and most important factor in preventing adolescent drug use," Dr. Szapocznik said. Typically, young people begin using drugs for one of two reasons: in response to social norms or because they are troubled, Dr. Szapocznik noted. "For adolescents, social norms are a tide that lifts all boats," he said. "Kids respond to an environment in which drug use is accepted or glamorized by taking drugs. Troubled kids use drugs because they want to feel better."

The key to preventing drug use is a family environment marked by open communication, effective management of complex social and academic issues confronting young people, and a clear message that drug use is harmful and unacceptable, Dr. Szapocznik said. NN

"NIDA is the world's leading brain trust on the causes and consequences of drug abuse. This is a remarkable legacy, combining rigorous science and human compassion to loosen the grip of drug addiction. NIDA has helped clarify how and where drugs work in the brain to cause their addictive effects. NIDA has provided complex models to improve treatment and rehabilitation strategies. The Institute has produced groundbreaking work on nicotine addiction.

"These are critical discoveries of science, but they don't do justice to the deeper nature of NIDA's work—the human element. Thanks to NIDA's bold and brilliant work, we are beginning to more clearly understand the lure of illicit drugs and how they seduce human beings into risking their health, the fabric of their relationships, their very lives."

Secretary of Health and Human Services
Donna E. Shalala

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 5 (December 1999)

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

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.

IDUs recruited by peers were more representative of the racial and ethnic composition of the community. The 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 drugs 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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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 3 (September 1999)

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.

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 2 (August 1999)

Infectious Diseases and Drug Abuse

Drug abuse involves health risks that often are as dangerous as the physiological effects of the drugs themselves. Injecting drug users (IDUs) are at high risk for direct exposure to a variety of blood-borne bacterial and viral infections. As a result, drug users are more likely than nonusers to contract a variety of infectious diseases and, when infected, to progress to serious illness and death.

HIV/AIDS

Injection drug use has been responsible for more than one-third of all adult and adolescent AIDS cases reported in the U.S. since the beginning of the AIDS epidemic, according to the Centers for Disease Control and Prevention (CDC) in Atlanta. More than one-half of all preadolescent AIDS cases in the U.S. have resulted from a transmission chain whereby a woman contracts HIV as a result of injection drug use and passes the disease to her child during pregnancy or birth. Of adult and adolescent AIDS cases, approximately 32 percent were among IDUs, and another 4 percent involved heterosexual sex with an IDU. During 1998, approximately one-third of all new AIDS cases in the U.S. were related directly or indirectly to injection drug use (See chart for a breakdown of the injection drug use-related cases).

Noninjection drug use can also contribute to HIV transmission. Studies have shown that inner-city youths who smoke crack cocaine are up to three times more likely to be infected with HIV than are inner-city youths who do not. Noninjecting drug users who trade sex for drugs or who engage in unprotected sex while under the influence of drugs increase their risk of infection.

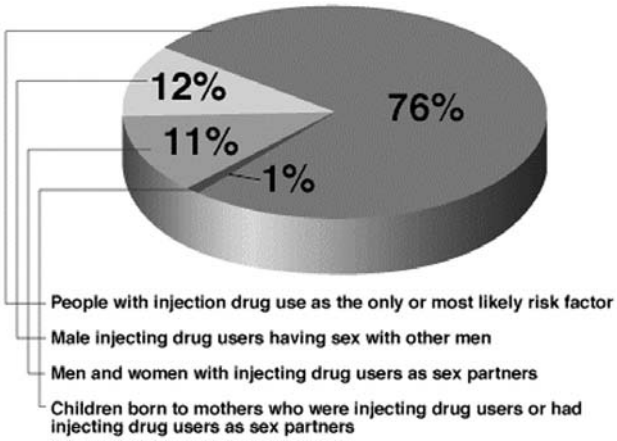
Hepatitis

Hepatitis B (HBV) and hepatitis C (HCV) are viral diseases that destroy liver cells and can lead to cirrhosis and liver cancer. People can become infected with HBV through sexual intercourse with an infected person or through exposure to an infected person's blood, as may happen when IDUs share needles. Blood transfusion and needle sharing are the most common routes of infection with HCV. NIDA-supported research has shown that the risk of infection by HBV and HCV is extremely high in the first year after beginning injection drug use. One study found overall HCV and HBV prevalences of 76.9 percent and 65.7 percent, respectively, in a group who had been injecting drugs for 6 years or less.

Tuberculosis

Tuberculosis (TB) is transmitted from person to person by airborne bacteria. This disease is most prevalent in crowded low-income areas with substandard health conditions. Drug users are from two to six times more likely to contract TB than nonusers. CDC estimates that in 1996 at least 11 percent of new TB cases were in drug users with noninjecting drug users twice as likely as IDUs to contract the disease. Compared to others with TB, IDUs are more likely to develop the disease in multiple organs and sites, rather than only in the lungs.

1998 AIDS Cases Related to Injection Drug Use



Other Infectious Diseases

Drug users have a high incidence not only of HIV/AIDS, but also of other sexually transmitted diseases including syphilis, chlamydia, trichomoniasis, gonorrhea, and genital herpes. The geographic distribution of syphilis and gonorrhea infections across the U.S. reflect the geographical distribution of the use of crack cocaine and its associated high-risk behaviors, such as unprotected sex and the exchange of sex for drugs.

Among IDUs, the most common cause for medical treatment is skin infection at the site of injection. Complications from these infections range from skin ulcers and localized abscesses to stroke, botulism, tetanus, destruction of lung tissue, and infection of the heart valves.

Bacterial and viral infections associated with injection drug use can progress to systemic infections and damage any body system. Directly observed medication therapy, in which the patient takes medications in the presence of a health care provider, is generally recommended for addicts, many of whom may have difficulty following treatment regimens. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 2 (August 1999)

New York City's Declining HIV Epidemic

The prevalence of HIV infection among injecting drug users (IDUs) in New York City has declined markedly. In a NIDA-funded study conducted with 11,334 IDUs, from 1991 through 1996, more than half tested negative for HIV over time. The study—conducted by Dr. Don Des Jarlais of the Beth Israel Medical Center in New York City; his colleagues from the National Development and Research Institutes, Inc., in New York City; the New York City Department of Health; the New York University School of Medicine; and the Centers for Disease Control and Prevention in Atlanta—looked at five ongoing studies over a 5-year period. At a citywide drug detoxification program, the portion of IDUs infected with HIV decreased from 53 percent to 36 percent. In a methadone maintenance program, the portion decreased from 45 percent to 29 percent. Two drug abuse research storefronts saw decreases in positive HIV test results, from 44 percent to 22 percent and from 48 percent to 21 percent. At a citywide network of sexually transmitted disease clinics, rates decreased from 30 percent to 21 percent.

The researchers theorize that the reduction of HIV among IDUs in New York City may be due to two major factors: the deaths of many HIV-infected IDUs and the reduction of risk behaviors, such as sharing drug paraphernalia. The researchers stress that the relative importance of these and other contributing factors must be studied further before any definitive conclusions about the reasons for the decline can be reached.

The Des Jarlais study team speculates that further reduction in risk behaviors among IDUs should result in further reduction of new HIV infections.

Source

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 2 (August 1999)

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.

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.

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.

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 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.

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.

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.

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.

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 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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 2 (August 1999)

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.

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

Previous studies have found higher rates of transition from noninjection to injection drug use, particularly among former injectors. However, Dr. Neagius 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,"

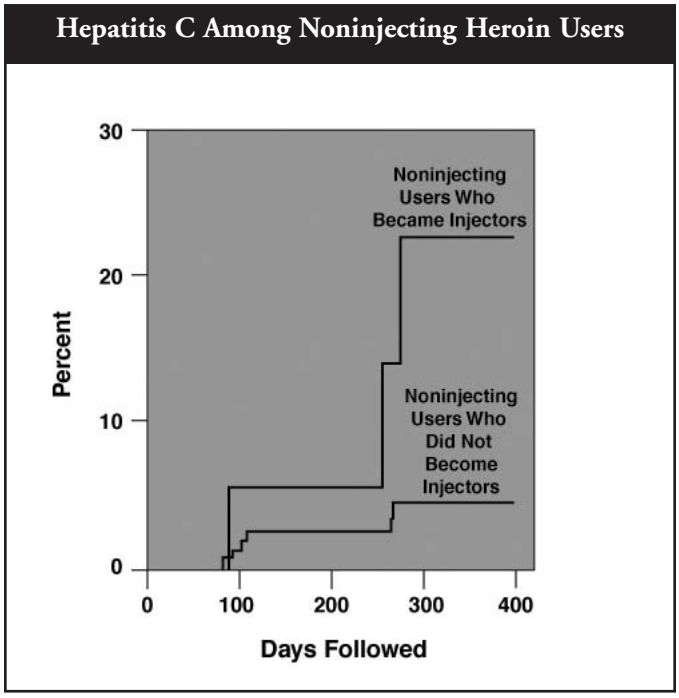
Dr. Neaigus says. "However, it is still alarming," he adds. What was unexpected was that some NIUs who did not begin to inject drugs—about 4 percent—also contracted HCV during the followup period. NDRI researchers now are attempting to determine how these NIUs contracted the infection, Dr. Neaigus says.

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.

> ***"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**

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.

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 noninjecting heroin users who transitioned to injection drug use contracted the disease.

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.

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 14, Number 1 (April 1999)

NIDA's Report Card

Each year at the NIDA Constituent Conference, representatives of national groups in the field of drug abuse provide advice and feedback to the Institute. During the meeting, participants recommend to NIDA staff activities that they think the Institute should undertake to advance its mission. At the next constituent conference, NIDA reports on the actions it has taken in response to the input from constituents. NIDA calls this detailed list of activities its "Report Card."

NIDA's 1998 Report Card lists 139 activities that address constituents' recommendations. A sampling of these activities is listed below.

- Sponsored the "National Conference on Drug Addiction Treatment: From Research to Practice," in Washington, DC, in April 1998. The conference highlighted more than 20 years of research on drug addiction treatment and was attended by leaders of national drug abuse organizations, related organizations, treatment practitioners, the media, and the public.
- Published two new cocaine treatment manuals: *A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction* and *A Cognitive-Behavioral Approach: Treating Cocaine Addiction*. These manuals are available at no charge. Two additional treatment manuals are currently being written: *Treating Cocaine Dependence With a Group Drug Counseling Approach* and *Treating Cocaine Dependence With an Individual Addiction Counseling Approach.*
- Continued its "Town Meetings" series with meetings in Boston and Des Moines, Iowa, in 1998. At these events, Dr. Leshner and NIDA researchers provide information and guidance to help State and local organizations, policymakers, and communities assess their local drug problems and develop specific programs to address these problems.
- Released a Community Drug Alert Bulletin on methamphetamine at the Des Moines Town Meeting in October. This bulletin highlights the current understanding of methamphetamine as a public health threat.
- Published Drug Addiction Research and the Health of Women and its companion Executive Summary and posted these documents on the NIDA Web site. At this national conference in 1994, leaders in women's health addressed the issues of drug abuse by women from historical, epidemiologic, biological-behavioral, and legal perspectives.
- Launched NIDA Infofax, a mail/phone/fax information retrieval system accessed via a toll-free telephone number. NIDA Infofax offers free, accurate information on drug abuse and addiction in English, Spanish, or TTY, toll-free, 24 hours a day. Callers can receive fact sheets and news releases by fax or mail, or hear recorded messages about the health effects of specific drugs, drug abuse and AIDS, prevention and treatment, and nationwide trends. Infofax is the first network-based system of its kind at NIH.
- Published *Assessing Drug Abuse Within and Across Communities*, which is designed to help communities understand their local drug abuse problems and develop epidemiologic surveillance systems to assess local drug abuse patterns and trends.
- Established the Center for AIDS and Other Medical Consequences of Drug Abuse to address the role of drug abuse as the leading risk factor for new cases of HIV infection and other infectious diseases, such as hepatitis and tuberculosis.
- Proposed the establishment of the National Drug Abuse Treatment Clinical Trials Network to conduct large, rigorous, statistically powerful, controlled, multisite treatment studies in community settings with diverse patient populations.
- Developed a new publication, *Economic Costs of Alcohol and Drug Abuse in the United States*, in collaboration with the National Institute on Alcohol Abuse and Alcoholism. The report provides the most current findings and interpretations of data in the areas of cost and cost analysis.
- Launched the Vulnerability to Addiction Initiative to explore why some people are more likely than others to abuse drugs.
- Is establishing Transdisciplinary Tobacco Use Research Centers in partnership with the National Cancer Institute to support research on tobacco use initiation, addiction, cessation, and prevention. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 5 (February 1999)

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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 5 (February 1999)

Global Network Will Promote Information Exchange On HIV Prevention in Drug-Using Populations

By Barbara Cire, *NIDA NOTES* Associate Editor

An international research network to facilitate rapid international exchange of information on HIV patterns and trends in drug-using populations was established at a NIDA-sponsored meeting in Geneva, Switzerland, in June. NIDA created the Global Research Network on HIV Prevention in Drug-Using Populations in collaboration with the World Health Organization's Programme on Substance Abuse (WHO/PSA) and the Joint United Nations Programme on HIV/AIDS (UNAIDS).

"The Network will enable researchers, policymakers, and public health practitioners around the world to share information about research design and methodologies, as well as effective intervention strategies to prevent the spread of HIV," says Dr. Richard Needle, chief of NIDA's Community Research Branch. Dr. Needle took the lead in planning, organizing, and chairing the meeting. "Numerous HIV prevention and risk reduction programs are being implemented effectively in countries around the world. What is lacking is an expanded, coordinated, structured exchange of information about research and policy related to preventing HIV/AIDS in drug-using populations."

The need for an international forum for countries to share information on drug use and HIV/AIDS was identified at a NIDA research synthesis symposium in Arizona in 1997 at which scientists reviewed more than 10 years of research on HIV in drug-using populations. The scientists concluded that the HIV epidemic could be slowed among these populations, but that the exchange of information was crucial to the effort.

At the Geneva meeting, participants discussed the possibility of establishing an interactive electronic system. The system would use Internet links, e-mail, and other methods to rapidly disseminate scientific findings and effective HIV risk-reduction strategies to scientists and public health professionals around the world. As more solid, science-based research is conducted and shared, more effective interventions will be possible, the participants concluded.

More than 60 researchers and public health professionals from 21 countries attended the inaugural meeting of the Global Research Network, which was held in conjunction with the 12th World AIDS Conference. Participants presented overviews of HIV epidemiology and prevention research in their countries. They also reported on the organizational infrastructures and financial mechanisms that support their drug abuse and HIV/AIDS research activities.

Worldwide, 129 countries and territories now report injection drug use, with 108 countries reporting HIV or AIDS in the drug-using population, according to the World Health Organization. In the United States, approximately one-half of the 41,000 new HIV infections each year

Researchers From 21 Countries Launch Global Network

Countries represented at the first Global Research Network meeting included Argentina, Australia, Brazil, Canada, China, Colombia, Dominican Republic, Egypt, Hungary, India, Kazakhstan, Malaysia, Mexico, Netherlands, Nigeria, Portugal, Slovak Republic, Switzerland, United States, United Kingdom, and Vietnam.

occur among injecting drug users, their sexual partners, and their offspring. In Argentina, 36 percent of the HIV/AIDS cases are associated with injection drug use, and in Uruguay 26 percent are, according to UNAIDS data. In Asia, injection drug use is the major mode of HIV transmission, representing more than 80 percent of HIV cases in Kazakhstan, 75 percent in Malaysia, 75 percent in Vietnam, and 50 percent in China, said Dr. Andrew Ball, Medical Officer, Treatment and Care, of WHO/PSA. Injection drug use also is the major mode of HIV transmission in North Africa, Eastern Europe, the former Soviet Union, and the Middle East, Dr. Ball said.

"NIDA-funded research in the United States has demonstrated that interventions to reduce the risk of HIV in drug-using populations can be effective," says Dr. Needle. "Through international collaboration in surveillance, prevention, and treatment of drug abuse and its consequences, we can look forward to introducing, adapting, and sustaining effective HIV prevention principles and programs in the global arena."

For More Information

To learn more about the Global Research Network, contact Dr. Richard Needle at (301) 443-6720; fax: (301) 480-4544; e-mail: rn28e@nih.gov. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 5 (February 1999)

New NIDA Center Will Address Health Issues Associated With Drug Abuse

By Barbara Cire, *NIDA NOTES* Associate Editor

NIDA has established a new center to coordinate research, collaborate with other of the National Institutes of Health (NIH) institutes and related organizations, and provide leadership to NIDA offices and divisions on issues about HIV/AIDS and other medical consequences of drug abuse. The Center for AIDS and Other Medical Consequences of Drug Abuse, headed by Dr. Henry Francis (above), was established through a merger of NIDA's Office on AIDS and Clinical Medical Branch, but its mission and responsibilities go beyond those of these two components.

"The new Center represents an important initiative to increase NIDA's multidisciplinary drug abuse research," says NIDA Director Dr. Alan I. Leshner. "The Center will allow us to address the full spectrum of health issues associated with drug abuse, including HIV/AIDS."

The Center will develop multidisciplinary national and international programs on HIV/AIDS; the medical, health, and developmental consequences of drug abuse; and the effects of drug use on other diseases. Program areas include the origins, treatment, and prevention of hepatitis C; HIV disease progression; the links between drug abuse treatment and medical care; tuberculosis in drug users; clinical research on human development and drug abuse; and prescription drug abuse.

"The connection between HIV/AIDS and injection drug use is well-known," says Dr. Francis. "Now is the time to step up our examination of that connection as well as the connections between drug abuse and other diseases related to drug abuse, including hepatitis, tuberculosis, hypertension, and sexually transmitted diseases in addition to AIDS. A number of mental health conditions also are associated with drug abuse, including severe depression, schizophrenia, personality disorders, and manic-depressive disorder. Sometimes mental health problems precede drug abuse, but in other cases they co-occur with drug abuse. It is important to address the impact of these disorders on drug abuse and the impact of drug abuse on these disorders."

The Center is currently supporting several collaborative studies with other NIH Institutes and government agencies, as well as nongovernment groups. For example, NIDA is participating in the Women's Interagency HIV Study/HIV Epidemiology Research Study with the National Institute of Allergy and Infectious Diseases (NIAID), the National Cancer Institute, the National Institute of Child Health and Human Development (NICHD), the National Institute of Dental and Craniofacial Research, and the Centers for Disease Control and Prevention. This study is examining the medical and psychosocial impact of HIV on women. NIDA is also collaborating with NIAID and NICHD on the Women and Infants Transmission Study, which is investigating mother-to-infant transmission of HIV.

"Drug addiction is a cross-over disease that permeates virtually all of the research areas addressed by NIH," says Dr. Francis. "Thus, a multidisciplinary approach is best suited to exploring the health aspects of drug abuse."

Prior to this appointment, Dr. Francis served for 2 years as chief of the Clinical Medicine Branch in the Division of Clinical and Services Research at NIDA. He was the director of the U.S. Public Health Service and Belgium Projet SIDA (Project AIDS) Research Laboratories in Kinshasa, Zaire, from 1984 to 1988. Dr. Francis received his medical degree from Howard University College of Medicine and performed his clinical training in internal medicine at the Long Beach Veterans' Administration Department of Medicine at the University of California at Irvine. He was a fellow, and later assistant professor, in the Division of Infectious Diseases at The Johns Hopkins Medical School. He is widely published and has written articles on HIV/AIDS that have appeared in the *Journal of the American Medical Association*, *Lancet*, the *New England Journal of Medicine*, the *Journal of Immunology*, and the *Journal of Infectious Diseases*, among others. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

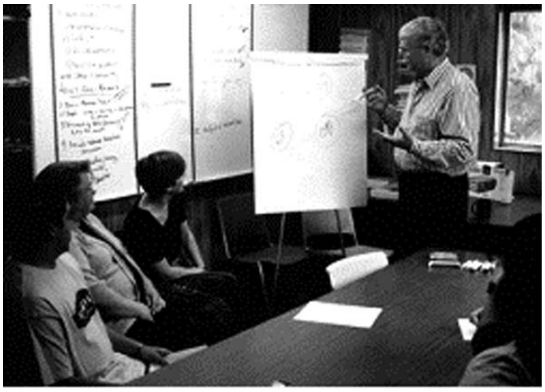
Research Findings

Volume 13, Number 4 (November 1998)

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 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.

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.

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.

Source

- Trotter, R.T.; Bowen, A.M.; Baldwin, J.A.; and Price, L.J. The efficacy of network-based HIV/AIDS risk-reduction programs in midsized towns in the United States. *Journal of Drug Issues* 26(3):591–605, 1996. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 4 (November 1998)

Gender Matters in Drug Abuse Research

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

Accumulating evidence indicates that drug abuse may begin and progress differently, have different consequences, and require different prevention and treatment approaches for women and men. Therefore, NIDA has strongly supported research to identify gender differences and gender-specific aspects of drug abuse and addiction and to apply these findings toward more effective drug abuse prevention, treatment, and services for both women and men.

Historically, NIDA has supported a broad program of research on the effect of women's drug use on pregnancy, maternal health, and childhood development. A little more than 5 years ago, NIDA broadened the scope of its gender-related research by issuing program announcements calling for research to examine the causes and consequences of drug abuse among women of all ages, regardless of their parental status. In the fall of 1994, NIDA sponsored a landmark national conference on addiction and women's health. This meeting launched our expansion of research on the role of gender in all aspects of drug abuse and addiction. Since then, our Women and Gender Research Group, which is made up of representatives from every NIDA Division and Office, has been working to further develop NIDA's research on women's health and gender differences and to disseminate the findings to professionals in the field and the general public.

In the last 5 years, NIDA has greatly increased scientific knowledge about gender-related differencs in almost every aspect of drug abuse and addiction.

Today, gender-related research is integrated throughout NIDA's entire portfolio. This research extends from basic molecular and cellular studies to clinical and epidemiologic studies and is grouped into four major areas: etiology, consequences, prevention, and treatment and services. Through this research, we are learning more and more about differences between women and men in the origins of drug abuse, the consequences of drug abuse and addiction, and the factors that influence drug abuse relapse and recovery.

Our research on the origins of drug abuse has found gender differences in factors affecting initiation, progression, and maintenance of drug use. For example, basic behavioral and neurochemical research has suggested that women may be more sensitive than men to the rewarding effects of drugs, perhaps due to differences in brain chemistry. Animal studies also have shown that females respond more than males to the stimulating and reinforcing properties of abused drugs. Other studies indicate that the intensity of a drug's effects on women varies during different phases of the menstrual cycle. These physiological differences may help account for data indicating that women may proceed to drug abuse and addiction more rapidly than men do after initial drug use.

Evidence also indicates that psychosocial factors, such as childhood physical and sexual abuse, depression and posttraumatic stress disorder, relationships with a significant other, and partner violence play a more important role for women than for men in beginning and continuing drug use. For example, one research study suggests that women's tobacco use is controlled more by social and sensory factors and less by dependence on nicotine itself, compared to men's tobacco use.

NIDA-supported research also is finding gender differences in the consequences of drug abuse. For example, both animal and human studies indicate that men may be at greater risk than women for strokes and for mental deficits from chronic cocaine abuse. Other research suggests that the female hormone estrogen may play a role in reducing cocaine toxicity in women.

One of the most devastating health consequences of illicit drug use for both women and men is AIDS, with half of all new HIV infections now linked to injection drug use. Approximately two-thirds of AIDS cases in women and more than half of pediatric AIDS cases in the United

States are related to injection drug use by women or their sexual contact with an injecting drug user.

NIDA's comprehensive AIDS initiative is uncovering significant gender-related differences in factors that contribute to and protect from HIV risk. For example, one study of female injecting drug users has found that the family plays a more important role for women than for men in resistance to needle-sharing behaviors.

Other studies in our AIDS research portfolio are identifying gender-specific strategies to decrease injection drug use and high-risk sexual behaviors among women and men. For example, researchers at Northern Arizona University in Flagstaff have found that male drug abusers are more likely to reduce their high-risk sexual behaviors if given HIV risk-reduction information on the street, while female drug abusers respond better if this information is given along with counseling in the more protective environment of an office.

Through this research, we are learning more and more about differences between women and men in the origins of drug abuse, the consequences of drug abuse and addiction, and the factors that influence drug abuse relapse and recovery.

The ultimate goal of our research is to apply our increased understanding of gender-specific drug abuse factors to the development of prevention and treatment interventions that better meet the unique needs of both women and men. For example, a recent NIDA-supported study indicates that treatment interventions need to address differences in psychosocial factors that influence women's and men's relapse to drug use following treatment. In the study, researchers at the University of Pennsylvania found that negative emotions and interpersonal relations are linked to relapse among cocaine-dependent women while men are more likely to experience positive emotions prior to relapse.

In the last 5 years, NIDA has greatly increased scientific knowledge about gender-related differences in almost every aspect of drug abuse and addiction. However, we still have tremendous gaps to fill in that knowledge. We need to learn more about how gender relates to the impact of violence and victimization, devise better gender-specific treatment for comorbid mental disorders, and learn how to adequately address gender-related cultural factors in prevention and treatment, to name just a few.

To fill those gaps and build on our current knowledge, we are encouraging research that addresses gender-specific issues and gender differences in such diverse drug abuse areas as origins and pathways, biomedical factors, comorbid mental disorders, epidemiology, medical and health consequences, health services, special populations, HIV/AIDS, prevention, and treatment.

Evidence from NIDA's gender-related research indicates that prevention and treatment strategies that address gender differences can be more effective than one-size-fits-all approaches in preventing drug abuse and relapse following treatment. Through our continued strong emphasis on the role of gender throughout our research portfolio, NIDA is working to speed the day when gender differences are successfully addressed in all areas of drug abuse prevention and treatment.

For More Information

An overview of NIDA's research program on women's health and gender differences, details of research advances and opportunities, program announcements, publications, and research reports can be found under "Women's Health and Gender Differences," on NIDA's home page on the World Wide Web at www.nida.nih.gov. Information about women and drug abuse also is available from Infofax, NIDA's automated information retrieval system, at 1-888-644-6432. In addition, the "Bulletin Board" includes a description and ordering information for a recently released NIDA publication, Drug Addiction Research and the Health of Women. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 4 (November 1998)

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

By Neil Swan, *NIDA NOTES* Staff Writer

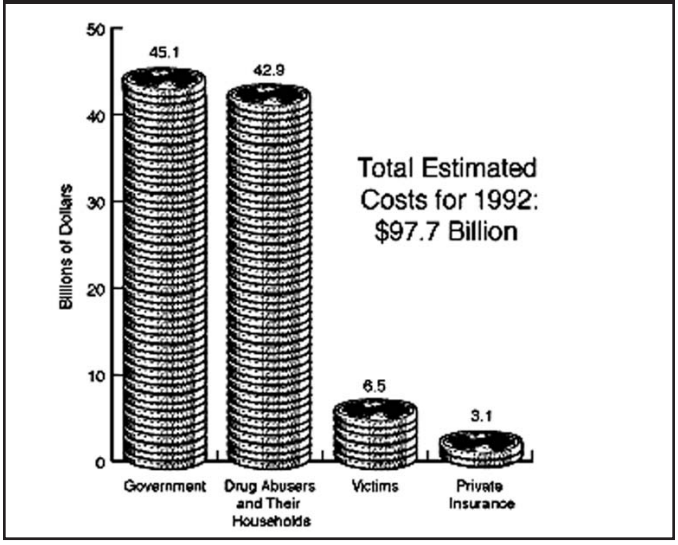
The economic cost to U.S. society of drug abuse was an estimated $97.7 billion in 1992, according to recent calculations. The new cost estimate continues a pattern of strong and steady increase since 1975, when the first of five previous cost estimates was made. The current estimate is 50 percent higher 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 caculated that the cost of drug abuse increased 12.5% from 1992 to 1995, bringing the cost to $109.8 billion in 1995.

Who Bears the Cost of Drug Abuse?



"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.

Changes in the methodology used to calculate estimates resulted in higher cost estimates for various health problems

Estimated Economic Cost of Drug Abuse in the United States, 1992 (millions of dollars)

Health Cost	
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 Costs	**$97,659**

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 rehabilitation 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 government 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 free from the National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20847, 1-800-729-6686. The study is also available on NIDA's home page on the World Wide Web at http://www.nida.nih.gov/EconomicCosts/Intro.html NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 3 (July 1998)

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

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 3 (July 1998)

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 "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

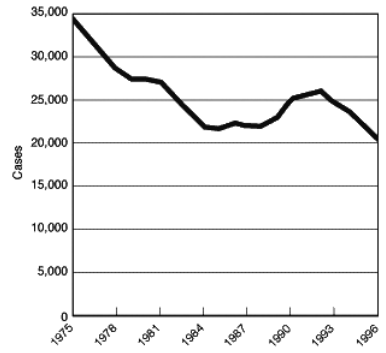
After decades of decline, tuberculosis (TB) re-emerged during the 1980s to mount a new threat to the Nation's public health. From a low of 22,201 cases in 1985, TB rates started to increase in the remaining years of the decade, according to the Centers for Disease Control and Prevention (CDC). The rise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

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



Source: Center for Disease Control and Prevention

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.

"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.

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 3 (July 1998)

Drug Addiction Treatment Conference Emphasizes Combining Therapies

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug addiction can often be treated best through a combination of behavioral and pharmacological treatments and social service interventions, according to speakers at NIDA's National Conference on Drug Addiction Treatment. The conference, held in Washington, DC, in April, attracted more than 800 drug abuse treatment researchers and service providers, leaders of professional organizations, criminal justice and law enforcement personnel, representatives from State drug abuse agencies, and public policymakers. The conference was presented as part of NIDA's Treatment Initiative, which is designed to improve the quality of the Nation's drug abuse treatment (see "NIDA Launches Drug Abuse Treatment Initiative," *NIDA NOTES*, July/August 1997).

At NIDA's treatment conference, Dr. Kathleen Carroll of Yale University describes how cognitive behavioral therapy can help patients learn to avoid situations in which they are likely to use cocaine.

Research is showing that drug addiction therapy that combines different approaches is often more effective than therapy that uses only one approach, said NIDA Director Dr. Alan I. Leshner. "When all is said and done, the ultimate cure for drug addiction will probably involve a combination of biological and behavioral treatments and social services," he said.

This approach of treating drug addiction by combining biological and behavioral therapies stems in part from studies showing that addiction is both a biological and a behavioral disorder, Dr. Leshner said. "What science has taught us is that drug addiction is a result of an interaction between an individual's biological vulnerability, plus his or her experiences, plus environmental factors plus, of course, drugs. The final result is a changed brain," he said. Viewing drug addiction as exclusively biological or behavioral is too limiting, he cautioned. "Let us not pit biology against behavior. These are not opposing viewpoints."

Combining medications with behavioral treatments can have an additive effect on therapy because the different treatments work on different aspects of addiction, said Dr. Bruce Rounsaville of Yale University in New Haven, Connecticut. Medications, such as methadone or medications that treat psychiatric disorders, can increase the chances that patients will stay in treatment. Psychotherapy can then help motivate patients to abstain from drugs and help them develop healthier lifestyles, said Dr. Rounsaville.

Several speakers examined behavioral therapies that are proving effective in treating drug addiction. Dr. Kathleen Carroll of Yale University School of Medicine described cognitive-behavioral therapy (CBT), a comparatively brief intervention that helps cocaine-dependent individuals become abstinent from cocaine and other substances. In CBT, patients learn to recognize and avoid the situations in which they are most likely to use cocaine. They also learn how to cope with their urges to use cocaine and to deal with their psychological, occupational, and other problems. "Drug use requires skills involving getting the money to buy drugs, getting the drugs, and other activities," said Dr. Carroll. "In CBT, the patient learns that he or she has the capacity to learn skills that are healthier and more productive," she said.

Another effective behavioral approach involves rewarding patients for staying abstinent, according to Dr. Maxine Stitzer of Johns Hopkins University in Baltimore. For example, patients can be given vouchers as a reward for drug-free urines. The vouchers can be exchanged for healthful goods or services valued by the patients.

In family therapy for drug addiction, the therapist suggests ways that family members can help their addicted relatives stop abusing drugs, said Dr. José Szapocznik of the University of Miami School of Medicine in Miami, Florida. In one situation, for example, a mother ordinarily may allow her adult drug-abusing daughter to stay with her for several days in between drug binges, despite her misgivings about the daughter's drug abuse. In family therapy, the therapist might encourage the mother to set limits for her daughter, such as allowing her to stay only if she agrees to remain abstinent. In addition to helping an addict, family therapy also has the potential for reaching other members of the family who may themselves have problems with drug abuse, said Dr. Szapocznik.

Dr. Herbert Kleber of Columbia University in New York City reported on detoxification techniques that help opiate addicts cope with withdrawal symptoms when they stop using opiates. Newer techniques include the use of a combination of the opiate treatment medications buprenorphine, clonidine, and naltrexone and the use of anesthesia or heavy sedation. Detoxification is only the first step in treating opiate addicts, Dr. Kleber stressed. "You should measure success not only by the level of comfort during withdrawal but also by how many patients go on for further therapy," he said.

At the conference, Dr. Mary Jeanne Kreek of Rockefeller University describes the health benefits of methadone treatment combined with behavioral treatments.

Other speakers discussed the challenges of providing drug abuse treatment for special populations. For example, individuals with both severe mental disorders, such as schizophrenia, and drug abuse disorders should be treated for both conditions concurrently, said Dr. Robert Drake of Dartmouth Medical School in Hanover, New Hampshire. This is best accomplished by multidisciplinary case management teams that might include a psychiatrist, a mental health case manager, a substance abuse specialist, and a vocational specialist who can address the patient's needs in an integrated fashion. This approach yields a number of benefits, including fewer relapses and hospitalizations and a higher functional status, said Dr. Drake.

Many drug-abusing adolescents also have a mental disorder, such as conduct disorder or depression, said Dr. Paula Riggs of the University of Colorado Health Sciences Center in Denver. These disorders contribute to the severity of the drug abuse disorder and should be treated concurrently, she said.

Drug abuse treatment can have health benefits in addition to reducing drug use, according to several speakers. Dr. David Metzger of the University of Pennsylvania in Philadelphia described numerous studies demonstrating that drug abuse treatment reduces the rates of HIV infection, by reducing both syringe sharing and risky sexual behaviors. Dr. Mary Jeanne Kreek of Rockefeller University in New York City presented data showing that, among injection drug users in New York City, methadone treatment, when combined with appropriate behavioral treatment, is reducing rates of both HIV infection and hepatitis B and, to a lesser extent, hepatitis C. Methadone treatment can also improve the health of addicts by normalizing immune function and the levels of stress and sex hormones, all of which are altered by drug abuse, Dr. Kreek said.

Thirteen million people in the United States currently abuse drugs, and 4 million are compulsive drug abusers, said General Barry McCaffrey, director of the Office of National Drug Control Policy, in the keynote address. The goal is to reduce the percentage of the U.S. population that is abusing drugs to under 3 percent by 2007, he announced. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 1 (June 1998)

Comparing Methamphetamine and Cocaine

Methamphetamine and cocaine belong to the broad class of drugs called psychostimulants that also includes amphetamine and methylphenidate. The two drugs often are compared to each other because they produce similar mood-altering effects and both have a high potential for abuse and dependence. Methamphetamine and cocaine also share other similarities. However, the two drugs also exhibit significant differences. Here are some of these similarities and differences.

Based on a year-long review of treatment research, Principles describes where we stand today in our quest for the most effective, replicable treatments for drug abuse.

Sources

- Methamphetamine is man-made.
- Cocaine is plant-derived.

Common Methods of Use

- Both methamphetamine and cocaine are commonly smoked, injected intravenously, or snorted.
- Methamphetamine also is commonly ingested orally.

Geographic Patterns of Use

- Methamphetamine use is highest in Honolulu, Hawaii, and western areas of the continental United States, particularly urban areas of California, Washington, Oregon, Colorado, and Arizona. In recent years, methamphetamine use has increased in both rural and urban areas of the South and Midwest. (Source: *Epidemiologic Trends in Drug Abuse: Advance Report*, 1997, NIDA.)
- Cocaine use shows no clear geographic pattern; regional rates of use vary from year to year. Cocaine use also is significantly higher in large metropolitan areas than in nonmetropolitan areas. (Source: Preliminary Results from the 1996 National Household Survey on Drug Abuse, Substance Abuse and Mental Health Services Administration.)

Euphoric Effects

- When they are smoked or injected intravenously, both methamphetamine and cocaine produce an intense, extremely pleasurable "rush" almost immediately, followed by euphoria, referred to as a "high."
- When snorted, both methamphetamine and cocaine produce no intense rush and take longer to produce a high; orally ingested methamphetamine produces a similar effect.
- Methamphetamine's high lasts anywhere from 8 to 24 hours, and 50 percent of the drug is removed from the body in 12 hours.
- Cocaine's high lasts anywhere from 20 to 30 minutes, and 50 percent of the drug is removed from the body in 1 hour.

Physical and Mental Effects

- The immediate effects of both methamphetamine and cocaine can include irritability and anxiety; increased body temperature, heart rate, and blood pressure; and possible death.
- Methamphetamine's and cocaine's short-term effects also can include increased activity, respiration, and wakefulness, and decreased appetite.
- Effects of chronic abuse of either methamphetamine or cocaine can include dependence and possible stroke.
- Chronic abuse of either methamphetamine or cocaine also can lead to psychotic behavior characterized by paranoia, hallucinations, mood disturbances, and violence. Anecdotal evidence suggests that violent behavior may be more common among chronic methamphetamine users than it is among chronic cocaine users.
- Drug craving, paranoia, and depression can occur in addicted individuals who try to stop using either methamphetamine or cocaine.

Neurotoxic Effects

- Methamphetamine is neurotoxic in animal species ranging from mice to monkeys; the drug damages the neurons that produce the neurotransmitters dopamine and serotonin. The usual doses taken by human methamphetamine abusers are comparable to the doses that produce neurotoxicity in animals.
- Cocaine is not neurotoxic to dopamine and serotonin neurons.

Transmission of HIV/AIDS

- Both methamphetamine and cocaine use contributes to transmission of HIV/AIDS through intravenous injection.
- Methamphetamine use in conjunction with high-risk sexual behaviors and cocaine use in "sex-for-crack" exchanges also contribute to transmission of HIV/AIDS. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 1 (June 1998)

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 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 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 **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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 13, Number 1 (June 1998)

NIDA Expands Research to Meet Challenge of Methamphetamine Abuse

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

Since the late 1980s, use of methamphetamine, a powerful central nervous system stimulant, has been a problem in western areas of the United States. More recently, NIDA's drug abuse monitoring systems and surveys show that use of the drug has been increasing in these areas and spreading to other areas of the country.

To counter this serious threat to the public health, NIDA has launched a comprehensive Methamphetamine Initiative that is stimulating research to fill gaps in the scientific knowledge about the pharmacology, toxicity, epidemiology, prevention, and treatment of methamphetamine abuse. At the same time, the Initiative is providing the public and health care practi-tioners with the latest available research information about methamphetamine to enable them to take action against methamphetamine use.

The Initiative will provide the additional scientific knowledge we need to develop more effective prevention and treatment approaches that can help communities respond to this complex public health problem.

The Methamphetamine Initiative builds on and complements the substantial body of knowledge yielded by previous NIDA-supported methamphetamine research. That research shows that smoking, snorting, ingesting orally, or injecting methamphetamine produces a long-lasting euphoria by stimulating excessive levels of the neurotransmitter dopamine in areas of the brain related to pleasure. Use of this powerful stimulant is associated with serious health consequences including addiction, memory loss, and potential heart and brain damage. Other damaging effects of use include aggression and violent and psychotic behavior. In addition, methamphetamine use is associated with increased transmission of hepatitis and HIV/AIDS.

We launched our Methamphetamine Initiative in San Francisco with a regional symposium on methamphetamine abuse, prevention, and treatment issues in December 1996. This symposium was an important step toward one of NIDA's most important goals for the Initiative—to translate the knowledge developed through research into a better public understanding of methamphetamine abuse and the implementation of more effective methamphetamine prevention and treatment strategies in the community.

Last year, NIDA received $4.2 million from the White House Office of National Drug Control Policy to broaden our ongoing program of methamphetamine research. This year, the Director's Office of the National Institutes of Health awarded NIDA an additional $2 million in special funds for additional methamphetamine research. The funds were devoted particularly to the development of new medications for methamphetamine overdose and addiction.

Our Initiative includes basic animal and human neuroimaging studies that will increase our understanding of the neurobiological mechanisms and consequences of methamphetamine use. Previous research has shown that prolonged exposure to relatively low levels of methamphetamine can damage as much as 50 percent of the dopamine-producing nerve cells in the brains of animals. NIDA-funded scientists now are studying whether, as we suspect, similar damage occurs in the brains of humans. These researchers also are looking at how such brain damage might affect the physiological functions and behavior of chronic methamphetamine abusers. One of the important questions this research will try to answer is whether such brain damage is linked to the hallucinations, paranoia, and violent behavior that sometimes accompany chronic methamphetamine use.

NIDA also is expanding its epidemiology research to help us answer questions about who is using methamphetamine and what promotes or inhibits the use of the drug. We need to know why methamphetamine use has been an

ongoing problem in the western United States and Hawaii but not in eastern cities. We need to identify factors that underlie the apparent recent spread of methamphetamine use to other areas of the country, including rural and urban areas of the South and Midwest. We also need to understand why methamphetamine use traditionally has been associated with white, male blue-collar workers and to determine what factors are now spurring its use by more diverse groups.

To answer such questions, NIDA recently launched a multisite study in cities where methamphetamine use is high and cities where use is low. The results of this research will provide the scientific base for developing more effective targeted methamphetamine prevention approaches. This will help forestall the spread of methamphetamine use and its harmful consequences to new groups and areas of the country.

Based on a year-long review of treatment research, Principles describes where we stand today in our quest for the most effective, replicable treatments for drug abuse.

We know that methamphetamine injection increases risk for contracting and transmitting HIV because injection drug use is a risk factor in nearly one-third of Americans infected with HIV. Furthermore, use of methamphetamine is associated with an increase in high-risk sexual behaviors that can contribute to the spread of HIV/AIDS. These behaviors represent a significant public health problem among gay and bisexual methamphetamine abusers in cities such as Los Angeles, San Francisco, and Seattle. Therefore, our Initiative is supporting a number of new and expanded studies to develop methamphetamine treatment interventions that target these populations. Using information gleaned from past treatment research, these studies are testing behavioral interventions, such as contingency management and relapse prevention. These approaches are designed to help modify methamphetamine abusers' thinking and behaviors, to increase their coping skills, and to reduce both methamphetamine abuse and associated HIV-risk behaviors.

In conjunction with our behavioral therapies development, the Initiative also is working to develop medications to reduce methamphetamine use. This effort is capitalizing on knowledge provided by our previous neurobiological research. We also are supporting research to develop medications that would ameliorate the harmful consequences of chronic methamphetamine abuse. For example, antidepressant medications are helpful in combating the depressive symptoms often seen in methamphetamine users who have recently stopped using the drug.

To help disseminate useful scientific information about methamphetamine abuse and its consequences that our research has given us, NIDA has developed a new research report on methamphetamine abuse and addiction. The report will provide the general public, policymakers, health care practitioners, and prevention and treatment service providers with an overview of the latest research findings on methamphetamine.

Recently, I was appointed to serve on a Methamphetamine Interagency Task Force, chaired by Attorney General Janet Reno and Office of National Drug Control Policy Director General Barry McCaffrey, that is working to enhance the Federal Government's education, prevention, and treatment practices and strategies to address methamphetamine abuse. The broad range of new research activities now being conducted under NIDA's Methamphetamine Initiative will provide the additional scientific knowledge we need to develop more effective prevention and treatment approaches that can be disseminated to help communities respond more effectively to all aspects of this complex public health problem. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 6 (November/December 1997)

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.

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

"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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 6 (November/December 1997)

Research Must Determine Medical Potential of Marijuana, NIH Expert Panel Concludes

By Robert Mathias, *NIDA NOTES* Staff Writer

A National Institutes of Health (NIH) panel of experts has concluded that critical questions about the therapeutic usefulness of marijuana remain largely unanswered by studies that have been conducted to date. The panel called for NIH to facilitate rigorous, well-designed clinical studies to evaluate marijuana's potential to treat a variety of medical conditions. Such studies must address the many potential short- and long-term hazards of smoked marijuana, the panel stressed.

The panel of eight experts, who have broad experience in clinical studies and therapeutics, expressed their opinions in a 37-page report that NIH issued in August 1997. NIH had convened the experts at a 2-day meeting earlier in the year to consider wide-ranging claims about the therapeutic usefulness of marijuana, particularly smoked marijuana, and the need for and feasibility of additional research. At the meeting, the panel reviewed the published scientific data on the medical use of marijuana and considered comments, including those from patients and advocacy groups.

Any studies of marijuana's medical potential need to consider both the short- and long-term risks associated with smoked marijuana, the panel stressed.

Under U.S. law, marijuana has been classified in the most restrictive category of controlled substances since 1970. This means that the drug in its usual form has a high potential for abuse and has no commonly accepted medical use in this country. However, advocates for the medical use of smoked marijuana claim it is effective in such areas as reducing nausea associated with cancer chemotherapy, counteracting the wasting syndrome associated with AIDS, and treating glaucoma. An oral form of marijuana's principal active ingredient, delta-9-tetrahydrocannabinol (THC), called dronabinol, is approved as a treatment for nausea and vomiting related to cancer chemotherapy. Dronabinol also is used to stimulate the appetite of AIDS patients.

The NIH panel noted that the current debate over using marijuana as a medicine centers on claims that smoked marijuana offers therapeutic advantages over dronabinol and that it has potential to treat other conditions, such as pain and glaucoma. However, little data from clinical trials are available to support or refute these claims, the panel's review showed.

Most previous studies of marijuana's therapeutic potential have used THC in capsule form. Such studies do not answer questions about the potential benefits or risks of smoked marijuana, which has substantially different dose absorption and pharmacological activity from the oral dosage form, the panel noted. In addition, although THC is the principal psychoactive component of the cannabis leaf, other compounds in the leaf may have therapeutic properties, the panel said.

The panel called for more studies to properly evaluate marijuana's medical potential in five areas: analgesia, or pain relief; neurological and movement disorders; nausea and vomiting associated with cancer chemotherapy; glaucoma; and appetite stimulation to counteract weight loss in patients with AIDS or cancer. In addition to dronabinol, effective treatments already are available for many of these indications, the panel noted. For example, a number of medications can treat pain without risking marijuana's adverse effects.

However, even where effective medications exist, marijuana could be studied for its potential to offer relief to patients who do not respond fully to such treatments, the panel stated. Other reasons for studying marijuana's medical potential include determining whether it is useful in treating diseases or conditions for which treatments are not currently available, such as nerve pain caused by disease or tissue injury, and whether it could enhance the therapeutic effects of currently available treatments.

Any studies of marijuana's medical potential need to consider both the short- and long-term risks associated with smoked marijuana, the panel stressed. Among the short-term risks cited by the panel are cardiovascular effects, effects on the lungs, and undesirable mental and behavioral effects. Other concerns would come into play if marijuana were used to treat patients with chronic diseases, such as the possibility that frequent and prolonged marijuana use might significantly impair the functioning of the body's immune system. Examining that aspect is particularly important for patients who already have compromised immune systems, such as cancer patients

undergoing chemotherapy and HIV/AIDS patients, the panel noted.

To address health concerns about using smoked marijuana for longer term therapy, the panel suggested that researchers strive to develop alternative dosage forms for marijuana, such as a smoke-free inhaled delivery system. Such a system could deliver purer forms of THC and related cannabinoids and permit better control of doses, the panel stated.

For More Information

The full text of the expert panel's report on the medical utility of marijuana is available at *http://www.nih.gov/news/medmarijuana/MedicalMarijuana.htm* NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 4 (July/August 1997)

NIDA Launches Drug Abuse Treatment Initiative

By Robert Mathias, *NIDA NOTES* Staff Writer

Several years ago, a NIDA-supported researcher in Vermont discovered that a new behavioral treatment could reduce cocaine abuse among mostly white rural patients. Later, when NIDA intramural and extramural researchers in Baltimore tested the same treatment with inner-city cocaine and heroin abusers, they found that it reduced their cocaine abuse, too. These researchers have shown that this behavioral treatment can reduce cocaine abuse among a variety of patients in controlled clinical research studies. However, they still have more to learn. For example, how well will the treatment work in a resource-starved neighborhood clinic? What training will treatment counselors need to use the new therapy effectively? Will the new treatment be cost-effective?

The Treatment Initiative will spur additional drug abuse treatment research and speed the evaluation and application of research-tested treatments in the real world.

How to translate promising drug abuse treatments from research into practice is one of the many critical issues that will be addressed by a major Treatment Initiative NIDA has launched to improve the quality of drug abuse treatment. The Initiative has both a research and a communications thrust. The research thrust will stimulate additional work to improve current treatments and to develop new treatments and transfer them to community-based drug abuse treatment clinics. The communications thrust will increase the exchange of useful information about drug addiction and its treatment among the research and treatment communities and the general public.

"We now have a variety of effective addiction treatments as a result of our research," says NIDA Director Dr. Alan I. Leshner. Both behavioral and pharmacological treatments have been shown to reduce drug abuse, crime and delinquency, and the spread of HIV/AIDS and other infectious diseases that are associated with drug abuse, he points out. "By spurring additional drug abuse treatment research and speeding the evaluation and application of research-tested treatments in the real world, NIDA's Treatment Initiative can have a significant impact on the Nation's public health," he says.

Under the research prong of the Initiative, NIDA will hold workshops to assess the current body of scientific knowledge about behavioral therapies, treatment medications, HIV/AIDS risk behaviors, and comprehensive treatment services. The Institute also plans to solicit and support new research to meet needs identified in all of these areas throughout the course of the Initiative.

Advancing the role of behavioral therapies in drug abuse treatment is a priority of the Treatment Initiative, says Dr. Lisa Onken of NIDA's Division of Clinical and Services Research (DCSR). Dr. Onken is coordinating the Initiative with Dr. Stephen Zukin, who heads the Division. This fall, DCSR is holding workshops on translating the findings of basic behavioral science research into innovative behavioral therapies and on transferring clinically tested behavioral therapies to the community treatment setting. Two other workshops are examining adolescent treatment issues. One is focusing on the development of more effective treatment approaches to deal with the special needs of adolescents. The other workshop is addressing how to develop early treatment strategies for adolescents and preadolescents who are beginning to abuse drugs.

Advancing health services research also will be an important part of the Initiative. This year, the Initiative is holding health services workshops on:

- factors that influence patients' readiness for treatment and motivation to change. This workshop also is exploring alternative approaches to drug abuse treatment for patients unable or unwilling to seek help in traditional treatment programs.
- drug abuse treatment for special populations such racial and ethnic minorities, the homeless, persons with disabilities, and pregnant women. Unique treatment needs, potential barriers to treatment, and culturally appropriate treatment models to set research priorities to improve treatment for these populations are among the issues on the agenda.
- integrating medical and mental health services and drug abuse treatment. This workshop aims to promote cross-system health services research by increasing communication and interaction between medical health services researchers and drug abuse treatment researchers.

- financing drug abuse treatmentand services. An expert panel is convening at this workshop to develop research recommendations to address both the immediate and long-term funding needs of providers of treatment resources.

Other Treatment Initiative research workshops on this year's agenda are designed to:

- evaluate the validity and reliability of instruments that researchers are currently using to assess whether drug abuse treatment reduces AIDS risk behaviors; and
- look at ways to improve and expand the use of the heroin treatment medication naltrexone.

Under the communications thrust of the Initiative, NIDA will hold a major drug abuse treatment conference in April 1998. The conference will highlight the principles of effective drug abuse treatment; detail pharmacological and behavioral treatments that have been shown to be effective; and examine the state of current research on special populations. The audience for the conference will include treatment researchers, treatment providers and practitioners, representatives from State drug abuse agencies and managed care organizations, and public policymakers. "We want to invite anyone who has an impact on treatment," said Dr. G. Alan Marlatt of the University of Washington in Seattle at a recent meeting of NIDA's National Advisory Council on Drug Abuse. Dr. Marlatt serves on a Council subcommittee that is helping NIDA plan the treatment conference and focus the Treatment Initiative.

In addition to the treatment conference, NIDA plans a host of other communications activities for the Initiative. Several work-shops will identify and disseminate research-based behavioral therapies. Additional conferences will update the drug abuse treatment community on the treatment of cocaine addiction, heroin treatment medications, and other effective drug abuse treatment and HIV prevention approaches. Treatment research symposia at major national meetings will inform professionals in related fields about drug abuse treatment research findings.

NIDA NOTES will provide further information about the Treatment Initiative's conferences, symposia, and workshops as details become available. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 2 (March/April 1997)

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:

- Shah, S.M.; Shapshak, P.; Rivers, J.E.; Stewart, R.V.; Weatherby, N.L.; Xin, K.-Q.; Page, J.B.; Chitwood, D.D.; Mash, D.C.; Vlahov, D.; and McCoy, C.B. Detection of HIV-1 DNA in needle/syringes, paraphernalia, and washes from shooting galleries in Miami: A preliminary report. *Journal of Acquired Immune Deficiency Syndromes* 11(3):301–306, 1996. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 2 (March/April 1997)

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, DC, 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 NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 2 (March/April 1997)

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. 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.

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

NIDA-funded research has clearly shown that drug abuse treat-ment 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 treat-ment 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 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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 1 (January/February 1997)

Constituents Help Shape NIDA's Research Agenda

By Margi Grady, *NIDA NOTES* Associate Editor

NIDA constituent groups have become instrumental in furthering the Institute's public health goals, NIDA Director Dr. Alan I. Leshner told participants at NIDA's Third Annual Constituent Conference in Lansdowne, Virginia, in November. In particular, Dr. Leshner praised the groups for working together at previous meetings to formulate recommendations for NIDA activities.

Constituent input has helped the Institute pursue its dual public health missions of conducting drug abuse research and disseminating the findings in a form that the drug abuse field and the public can use and understand, Dr. Leshner said. In return, the constituents have benefited because their recommen-dations have guided the Institute in funding research that addresses the real-world needs of the field, he noted.

In the 3 years since its inception, the Constituent Conference has helped focus and strengthen this advisory role for the constituent groups, Dr. Leshner said. The 2-day conference was attended this year by representatives from 48 national organizations involved in the field of drug abuse. The meeting included both general sessions and informal work groups in which participants met to prepare this year's recommendations to the Institute.

As evidence of the constituents' prominent role in guiding the Institute, Dr. Leshner presented a "report card" containing NIDA activities that address recommendations made by constituent representatives at previous conferences. The report card itemizes more than 300 activities that the Institute has undertaken in the broad areas of treatment research, HIV/AIDS research, prevention and epidemiology research, health services research, research training, information dissemination, and NIDA's organizational structure. Dr. Leshner highlighted several examples, including:

- funding 13 grants to study ways to link drug abuse treatment and medical care;
- planning a multicomponent treatment initiative for 1997 to improve the Institute's existing research portfolio and to take treatments shown to be effective in small-scale studies and evaluate them in large-scale clinical trials;
- issuing a request for applications calling for collaboration among universities, research institutes, and the pharmaceutical industry to expedite transition of preclinical research findings on cocaine therapies to clinical studies;
- establishing a program to provide supplemental funding to ongoing research projects at the National Institutes of Health for the study of issues related to drug abuse and HIV/AIDS;
- launching a methamphetamine research initiative and sponsoring a regional conference on methamphetamine to complement other national efforts to address increases in methamphetamine use in areas across the country;
- cosponsoring, with The Robert Wood Johnson Foundation, a National Conference on Drug Abuse Prevention Research;
- cosponsoring a meeting covering prevention and treatment research on child and adolescent substance abuse at the annual meeting of the American Academy of Child and Adolescent Psychiatry;
- funding new studies on the economics of treatment, barriers to access and utilization of treatment, translating new interventions into practice, and the cost-effectiveness of treatment;
- cosponsoring, with the American Psychological Association, the Conference on Drug Abuse (CODA) at the association's annual convention;
- holding several NIDA Town Meetings across the Nation to bridge the "great disconnect" between public perceptions and scientific facts about drug abuse;
- upgrading and expanding the NIDA home page on the World Wide Web;
- establishing the new NIDA Regional Neuroimaging Center at Brookhaven National Laboratory in Upton, New York, in collaboration with the White House Office of National Drug Control Policy and the U.S. Department of Energy; and
- expanding NIDA's National Advisory Council on Drug Abuse from 12 to 18 members.

"We were again pleased by the tremendous turnout for our conference," said Dr. Timothy P. Condon, NIDA's associate director for science policy, whose office organized the meeting. "These meetings provide the Institute with critical input to help us ensure that NIDA's research is relevant, user friendly, and used." NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 12, Number 1 (January/February 1997)

Smoking Any Substance Raises Risk of Lung Infections

By Michael D. Mueller, *NIDA NOTES* Staff Writer

Smoking any substance- tobacco, marijuana, or "crack," a smokable form of cocaine-increases a smoker's risk of developing bacterial pneumonia and other infections of the lungs, according to the findings of drug abuse, smoking and health, and AIDS researchers.

Although some drugs seem to have specific damaging effects when smoked, smoking anything appears to damage or paralyze the cilia, the hair-like projections in the lungs that sweep out microbes and other matter that can cause disease, according to NIDA-funded studies. Damaging the lung's cilia, the respiratory system's first line of defense, can have severe consequences for people with weak immune systems, the studies note.

Smoking anything appears to damage or paralyze the cilia, the hair-like projections in the lungs that sweep out microbes and other matter that can cause disease.

A NIDA workshop held in August 1995 examined current research at that time on the cardio-pulmonary complications of crack cocaine use. In a report summarizing the major findings presented at the workshop, Dr. Pushpa V. Thadani, a pharmacologist in NIDA's Division of Basic Research, notes that smoking cocaine appears to weaken the crack smoker's natural resistance to infection in the lungs.

"Pulmonary alveolar macro-phages-cells that protect the lungs from infectious agents-are exposed to the highest concentrations of cocaine," says Dr. Thadani. NIDA-funded studies show that alveolar macrophages from crack cocaine smokers are less active than are alveolar macrophages from nonsmokers in destroying Staphylococcus aureus, a common cause of bacterial lung infection. Preliminary findings also indicate that alveolar macro-phages of cocaine smokers are more susceptible to HIV-related infections than are alveolar macrophages of people who do not smoke cocaine.

"Much remains unknown about the effects of crack smoking on the alveolar macrophages and other cells of defense in the lungs," says Dr. Thadani. "However, it appears that there are profound effects, and this needs to be further explored," she says.

Dr. Donald P. Tashkin, a professor of medicine at the University of California at Los Angeles School of Medicine, and his colleagues recently examined the effects that habitual smoking of tobacco, marijuana, and/or cocaine has on the lining of the lung's air passages. The NIDA-funded study included 53 nonsmokers, 14 smokers of crack cocaine only, 40 smokers of marijuana only, and 31 regular tobacco smokers. In addition, there were 16 smokers of both cocaine and marijuana, 12 smokers of cocaine and tobacco, and 44 smokers of both marijuana and tobacco. Thirty-one patients smoked all three substances.

The researchers found that smoking either marijuana or tobacco produces significant damage to the cilia in the lining of the airways. Among smokers of both marijuana and tobacco, it appears that the effects of marijuana add to the effects of tobacco, and vice versa. "The damage to the ciliated cells in the lining of the airways caused by smoking tobacco, and/or marijuana weakens the ability of the lungs to remove inhaled particles, making the lungs more vulnerable to infection," says Dr. Tashkin.

Cocaine smokers had fewer significant abnormalities than marijuana or tobacco smokers did- but more abnormalities than were detected among nonsmokers, Dr. Tashkin says. Among people who smoke both tobacco and cocaine, cocaine smoking appears to produce injury to the mucosal lining of the airways beyond that caused by smoking tobacco alone.

A NIDA-supported study by Dr. Waleska T. Caiaffa and her colleagues at Johns Hopkins University in Baltimore compared the medical records of 40 HIV-positive injecting drug users (IDUs) who had suffered from one bout of bacterial pneumonia with those of 197 HIV-positive IDUs with no history of bacterial pneumonia. The study found that HIV-positive IDUs who smoked illicit drugs were almost twice as likely to develop bacterial pneumonia as were their counterparts who did not smoke illicit drugs. This association was independent of age, degree to which the natural immune system had been suppressed, and cigarette smoking. Among the 77 HIV-positive IDUs who reported smoking drugs, 87.9 percent indicated that they had smoked marijuana, 25.9 percent said that they had used cocaine, and 9.1 percent admitted smoking crack.

Smoking is a serious issue among AIDS patients, according to several NIDA-supported studies. The health effects of smoking illicit drugs are above and beyond those caused by smoking cigarettes, the studies note. People with AIDS often die of pneumonia and other lung problems, and smoking tobacco and/or illicit drugs increases the risks for these diseases.

"The effect that smoking has on the lungs is more serious than most people realize. Smoking anything is bad for your health, especially if your immune system has been weakened," says Dr. Tashkin.

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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 11, Number 4 (September/October 1996)

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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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 11, Number 4 (September/October 1996)

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.

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.

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.

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.

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.

"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.

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 compounding 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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NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 10, Number 6 (November/December 1995)

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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 10, Number 3 (May/June 1995)

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.

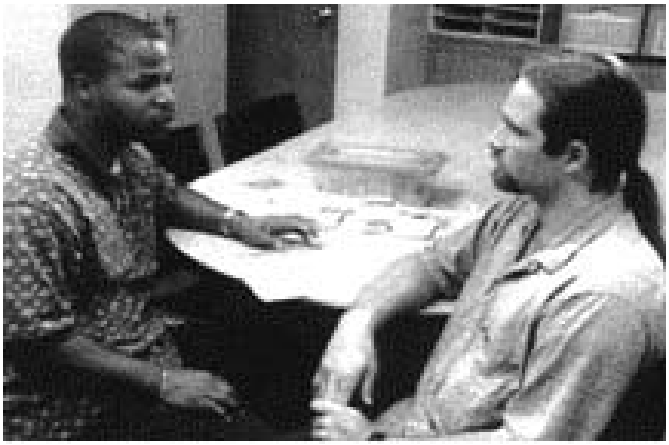
Subsequent NIDA-funded studies have reinforced these initial findings. University of Pennsylvania researchers studying heroin addicts in Philadelphia found that out-of-treatment subjects were injecting drugs, sharing needles, visiting shooting galleries, and practicing unsafe sex at significantly higher 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 risk-reduction education, counseling, and other strategies.

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.

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 per-cent of NADR participants reduced or stopped injecting drugs, 37 per-cent 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 per-cent before intervention to 19 per-cent 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 post-test 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 person's 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 per-cent 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 NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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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 NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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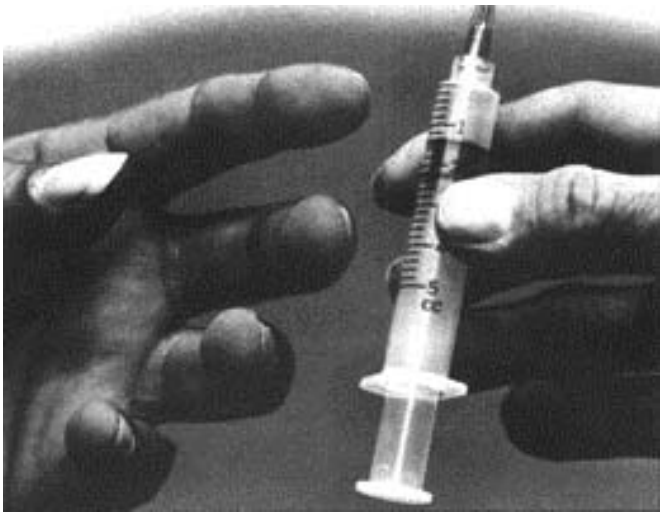
NIDA Plays Key Role in Studying Links Between AIDS and Drug Abuse

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 below).

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.

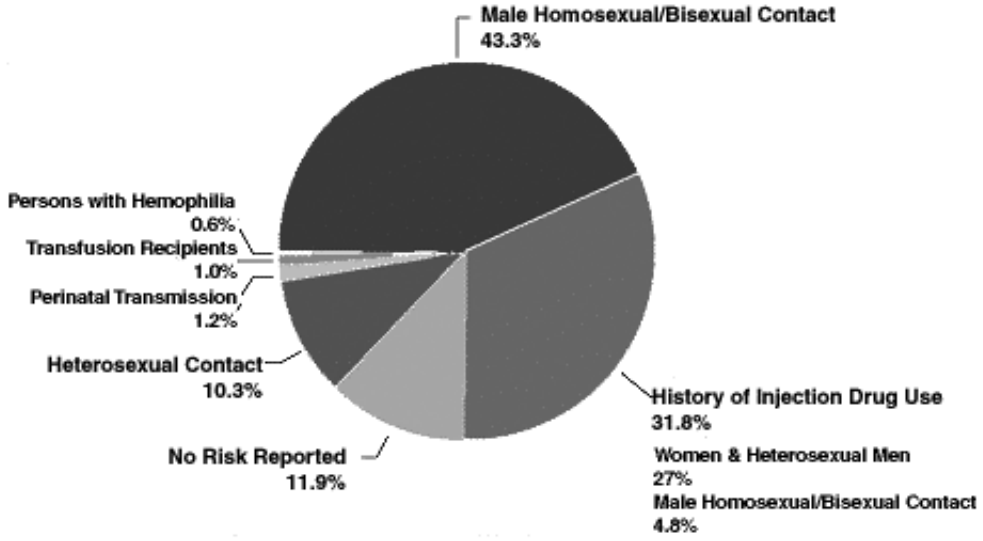
Because of this crucial link between AIDS and drug abuse, NIDA has played a critical role in the Government's strategy to control the spread of AIDS since early in the epidemic. Today, with a budget of $147 million for AIDS-related research, NIDA is the third largest supporter of AIDS research among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

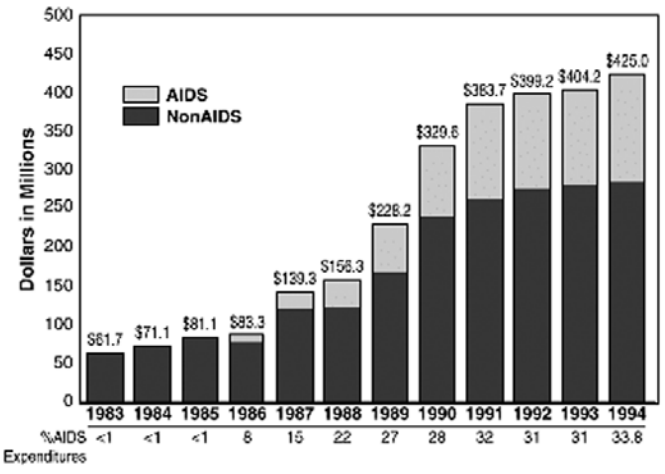
Reported U.S. AIDS Cases by HIV-Exposure Category—1994



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

(prevention and intervention) programs have been 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.

NIDA's AIDS and NonAIDS Expenditures



Source: NIDA Budget Office

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 NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 10, Number 3 (May/June 1995)

Institute of Medicine's (IOM) AIDS Research Recommendations

In a 360-page study mandated by Congress, the Institute of Medicine (IOM) makes 46 specific recommendations describing how NIDA and two other Federal agencies can broaden the scope of their AIDS-related behavioral studies. In the 1994 report, AIDS and Behavior: An Integrated Approach, the IOM commends NIDA on its record of AIDS research- multidisciplinary studies using various innovative combinations of pharmacologic, behavioral, and social approaches to improve the effectiveness of addiction treatment and outreach strategies for out-of-treatment addicts. The IOM recommended that the three Institutes- NIDA, the National Institute of Mental Health, and the National Institute on Alcohol Abuse and Alcoholism- intensify and coordinate their research into behaviors that contribute to the transmission of HIV, the virus that causes AIDS.

The IOM, with a membership of distinguished physicians and medical researchers, is a branch of the National Academy of Sciences, which advises Congress on health policy issues. Among the IOM's AIDS research recommendations are the following:

- collaborate to sponsor and conduct a nationwide survey of the prevalence of HIV infection and the behavioral and other factors associated with its spread;
- conduct studies of the social, psychological, and biological factors that affect HIV risk-taking behaviors;
- continue to develop studies of high-risk settings for drug abuse, such as shooting galleries and crack houses, that may contribute to the spread of HIV and AIDS, and help implement prevention efforts in those settings;
- expand basic research into the biology of sexuality as it relates to high-risk sexual behaviors and include studies of how the central nervous system controls sexual behavior;
- support research into changes in AIDS risk behaviors among seriously mentally ill men and women and those with other cognitive impairments, including individuals not in psychiatric treatment;
- continue supporting basic and applied research into the maintenance of behavior change, including how to prevent patients undergoing treatment for alcohol and drug abuse from relapsing;
- expand basic research into the biology of substance abuse, including the function of dopamine systems, the mechanisms and components of addiction-euphoria, tolerance, sensitization, and withdrawal-and the role of opioid receptors in drug addiction and abuse;
- design research to estimate the number of HIV infections averted by prevention efforts and the resulting savings in health care costs;
- develop new funding programs and grant review procedures to encourage innovative, collaborative, and cross-disciplinary research proposals;
- develop new initiatives to support research on the role of social, cultural, and structural factors in HIV and AIDS transmission, prevention, and intervention; and
- expand studies in the following behavioral and social science research areas: behavioral epidemiology research, cognitive science, cultural and ethnographic projects, intervention research, mental health research, behavioral aspects of technological interventions, organizational studies, cost-effectiveness research, and evaluation research. NN

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

Volume 10, Number 3 (May/June 1995)

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.

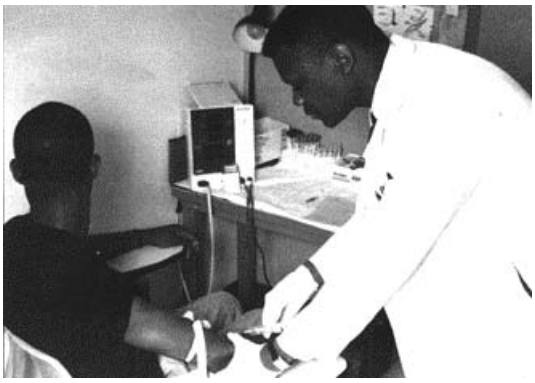
In a study of rhesus monkeys infected with simian immunodeficiency virus (SIV), an animal model for studies of HIV and AIDS, NIDA-supported researchers have shown that opioids increase the mutation of the virus in the early stages of SIV infection. These results suggest that, in humans, this type of 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.



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

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.

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

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Research Findings

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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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