

Cocaine Vaccine Helps Some Reduce Drug Abuse

A clinical trial encourages continued development of strategy based on immune system response.

BY LORI WHITTEN,
NIDA Notes Staff Writer

A vaccine to prevent cocaine abuse proved mildly effective in its first placebo-controlled test. Although their individual responses varied, vaccine recipients reduced their cocaine use more quickly than placebo recipients. A subgroup of vaccinated patients generated levels of antibodies that were sufficient to block cocaine's effects, and during the period of peak antibody production, they submitted more drug-free urine samples than participants in the placebo group or those who did not respond strongly to the vaccine. With further refinement to increase response, a vaccine might someday be available as a therapy for cocaine abuse, says lead investigator Dr. Thomas Kosten of Baylor College of Medicine in Houston.

TESTING THE CONCEPT

The cocaine vaccine consists of a small amount of the drug chemically bonded to a protein, derived from cholera toxin, that stimulates the immune system to produce antibodies (see illustration, page 6). Anti-cocaine antibodies latch onto cocaine molecules in the bloodstream, forming drug-antibody complexes that are too large to pass through the fine-grained tissue filter that enwraps and protects the brain. If the vaccinated person develops enough antibodies to capture and hold onto most of the cocaine molecules circulating in the blood, the

drug will not produce the euphoria or other psychoactive effects that reinforce drug taking and addiction.

For the first placebo-controlled test of the vaccine's ability to reduce cocaine use among people who are addicted to the drug, Dr. Kosten and colleagues recruited 115 men and women who were seeking treatment at an outpatient clinic after having abused cocaine for about 15 years. The study participants were taking cocaine, on average, three times daily, 3 days per week. All were also addicted to opioids and had initiated methadone maintenance therapy 2 weeks prior to their first dose of the cocaine

Anti-cocaine antibodies latch onto cocaine molecules in the bloodstream and keep them from entering the brain.

vaccine or placebo. The researchers chose this population because the patients came to the clinic daily to receive their doses of methadone, thereby increasing the likelihood that they would be available for injections, as well as urine and blood tests, and would remain in the study for its full 24-week duration.

Dr. Kosten and colleagues randomly assigned 58 patients to receive the cocaine vaccine in five intramuscular injections spaced over 12 weeks, a regimen that previous research had suggested should cumulatively produce enough antibodies to neutralize the amount of

ALSO IN THIS ISSUE

Research Findings

- 8** Study Supports Methadone Maintenance in Therapeutic Communities
- 11** Marijuana Linked With Testicular Cancer
- 13** Multidimensional Family Therapy for Adolescent Drug Abuse Offers Broad, Lasting Benefits

Director's Perspective

- 2** Incentives Promote Abstinence

Research in Brief

- 3** • Substance Abuse Among Women With Children • Deep Brain Stimulation Reduces Rats' Cocaine Seeking • Intervention Improves Abstinence, Employment Among Welfare Recipients

NIDA at Work

- 4** Workgroup Keeps NIDA on the Cutting Edge of Brain Science

Bulletin Board

- 16** • NIDA Appoints New Director of the Intramural Research Program • Addiction Science Awards Announced • Program Enhances Physician Knowledge on Substance Abuse • NIDA Grantee Wins Prize for Genetics Web Sites • Three Scientists Join Advisory Council

Update

- 18** • Parental Supervision and Genetics Interact To Influence Nicotine Addiction • Modafinil Normalizes Sleep During Early Cocaine Abstinence

Tearoff

- 19** NSDUH: Drug Abuse Levels Rising

What the Numbers Say

- 20** Prisons Lack Detox Services

[Continued on page 6]



Incentives Promote Abstinence

Staying the course and achieving abstinence in substance abuse treatment are two strong indicators that a patient is on the way to stable recovery. Patients who attend more therapy sessions gain more assets for long-term recovery, such as drug-avoidance skills and awareness of the benefits of healthy recreational activities and drug-free social networks. During drug-free intervals, patients accumulate experience in living without drugs.

Motivational incentives—tangible rewards for verifiable abstinence—are powerful tools for promoting both goals. In typical motivational incentive programs, patients receive vouchers for cash or goods each time they show up for a therapy session, pass a Breathalyzer test, or submit a drug-free urine sample. Studies have shown that substance abuse patients are better able to maintain desirable behaviors when they are rewarded daily or weekly rather than when they are asked to focus solely on the ultimate goal of long-term recovery. This accords with other research showing that addiction changes the brain in ways that make individuals more responsive to short-term rewards and less able to forgo them in the interest of longer term benefits.

Incentives extend abstinence during treatment for addiction to cocaine, methamphetamine, opioids, and nicotine, and they help cocaine abusers remain in treatment longer. Although the effectiveness of incentives tends to weaken after they are discontinued, some studies have found that benefits persist for 1 to 2 years.

Motivational incentives can promote and reinforce multiple healthy behaviors. For example, such interventions have improved drug abusers' adherence to HIV antiviral medication regimens and helped patients maintain regular exercise, job-hunting, and other activities that support a drug-free lifestyle. Investigators are currently examining how to tailor incentive programs for adolescents and pregnant women.

Motivational incentives need not strain budgets. NIDA-supported researchers have developed a program in which the rewards cost about \$200 per patient. Each drug-free sample earns the right to draw from a container of chips. Most of the chips say "good job" or can be traded for \$1 prizes, such as personal care products and bus tokens, but a few can be exchanged for prizes of greater value, such as music and video players. In a study conducted in the community-based facilities of the Clinical Trials Network, adding this program to usual care quadrupled the likelihood of stimulant abusers attaining 12 weeks of continuous abstinence. This is important because the longer patients are continuously abstinent, the greater their chances of maintaining future abstinence. NIDA hopes that these findings will encourage more clinics to adopt motivational incentives. ■

EDITOR

David Anderson
Public Health Advisor, Office of Science Policy and Communications, National Institute on Drug Abuse

DEPUTY EDITOR

Julie Ann Miller, Ph.D.
RTI International

MANAGING EDITOR

Andrew Keegan
RTI International

SENIOR SCIENCE WRITER

Lori Whitten, Ph.D.
RTI International

ASSOCIATE EDITOR

Debra P. Davis
RTI International

DESIGN/LAYOUT

Maggie Bray
RTI International

EDITORIAL BOARD

David Anderson, *Chair; Public Health Advisor, Office of Science Policy and Communications*

Nicolette Borek, Ph.D., *Research Psychologist, Division of Clinical Neuroscience and Behavioral Research*

Scott Chen, Ph.D., M.B.A., *Scientific Review Officer, Office of Extramural Affairs*

J.C. Comolli, *Public Health Advisor, Division of Pharmacotherapies and Medical Consequences of Drug Abuse*

Jennifer Elcano, M.A., *Science Writer, Office of Science Policy and Communications*

Lynda Erinoff, Ph.D., *Associate Director, AIDS Research Program, Division of Epidemiology, Services and Prevention Research*

Petra Jacobs, M.D., *Associate Director for Program Development, Center for Clinical Trials Network*

Jacqueline Lloyd, Ph.D., *Health Science Administrator, Division of Epidemiology, Services and Prevention Research*

Marsha F. Lopez, Ph.D., *Health Science Administrator, Division of Epidemiology, Services and Prevention Research*

Ivan Montoya, M.D., M.P.H., *Medical Officer, Division of Pharmacotherapies and Medical Consequences of Drug Abuse*

Mary Pfeiffer, Ph.D., *Editor and Writer, Intramural Research Program*

Kenzie Preston, Ph.D., *Chief, Clinical Pharmacology and Therapeutics Research Branch*

Paul Schnur, Ph.D., *Deputy Director, Division of Basic Neuroscience and Behavioral Research*

Anna Staton, M.P.A., *Public Health Analyst, Office of Science Policy and Communications*

Cora Lee Wetherington, Ph.D., *Psychologist, Division of Basic Neuroscience and Behavioral Research*

This publication was produced and printed by RTI International, under Contract No. HHSN271200900042C from the National Institute on Drug Abuse.



Substance Abuse Evaluated Among Women With Children

In two nationally representative surveys, about 2 percent of mothers with at-home children under the age of 18 reported symptoms meeting the clinical criteria for abuse of or dependence on illicit drugs or prescription drugs that are being misused.

Dr. Leigh Ann Simmons, currently of Duke University, and former colleagues at the University of Kentucky found that 1.1 percent of the 19,300 mothers in this category who responded to the 2002 and 2003 National Survey on Drug Use and Health had a substance use disorder involving prescription painkillers, tranquilizers, sedatives, or stimulants; 0.9 percent involving marijuana; 0.4 percent, cocaine; 0.1 percent, heroin; and 0.2 percent, multiple drugs. The overall rates of drug abuse were not higher among these women compared with other women who participated in the survey. Compared with non-drug-using mothers, however, mothers who used drugs were, on average, younger, less educated, more stressed,

less healthy, and more likely to be unmarried or divorced, unemployed, receiving public assistance, victims of interpersonal violence, and affected by serious mental illness.

Parental substance abuse increases a child's risk for neglect, abuse, and health and behavioral problems, including poor socialization, attention deficit hyperactivity disorder, depression, and substance use disorders. Dr. Simmons and colleagues urge increased attention to detecting and responding to parental drug abuse in primary care, pediatric, and emergency settings and support for research to better understand the impact of parental drug abuse and related factors on children's development.

> *Annals of Epidemiology* 19(3):187–193, 2009.

Deep Brain Stimulation Reduces Rats' Cocaine Seeking

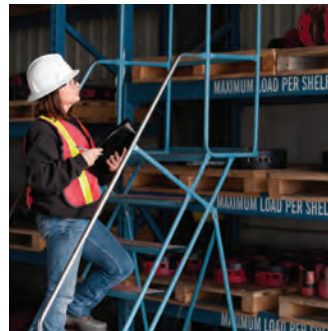
A stream of electrical pulses delivered to the brain's reward center curbs the power of a cocaine injection to spur rats to drug seeking.

Dr. R. Christopher Pierce of Boston University School of Medicine and colleagues trained rats to press a lever to self-administer the drug, then weaned the rats off that behavior by withholding the drug. Normally, after rats exposed to this protocol receive a priming injection of cocaine, they resume lever pressing, a

response that mimics human relapse to drug abuse. In the Boston experiment, rats that received 2 hours of deep brain stimulation to the shell area of the nucleus accumbens (NAc) immediately following the priming injection pressed the lever about half as much as control animals.

Dr. Pierce says his team's findings suggest that deep brain stimulation of the NAc shell holds promise as a therapy for severe cocaine addiction. Deep brain stimulation of a different brain region has benefited patients with Parkinson's disease, and the technique is also being tested as a potential therapy for severe depression that does not improve with medication.

> *Journal of Neuroscience* 28(35):8735–8739, 2008.



Intervention Improves Abstinence, Employment Among Welfare Recipients

Intensive case management (ICM) can help substance-abusing women who receive welfare benefits stay off drugs and make strides in employment, report Dr. Jon Morgen-

stern and colleagues at Columbia University. In a study of 302 applicants for Temporary Assistance for Needy Families in New Jersey, the researchers assigned roughly half to an ICM intervention that included weekly visits from a case manager, help in overcoming treatment barriers, assistance in identifying and meeting other patient service needs, and voucher incentives for remaining in treatment. The rest of the trial participants received the care welfare agencies typically provide to substance-abusing clients, which consists of screening and referral for treatment.

When interviewed after 24 months, 47 percent of the women receiving ICM had been abstinent from drugs for the past 30 days, compared with 24 percent of those in the usual care group. At that same time, 22 percent of the women in the ICM group—but only 9 percent of those in the usual care group—were employed full-time. For comparison, the full-time employment rate was 34 percent among 150 female welfare recipients who did not abuse drugs.

The researchers are now conducting a cost-benefit analysis of ICM. If their promising results are replicated in future evaluations, welfare agencies may have an effective tool to help some of their most vulnerable clients.

> *American Journal of Public Health* 99(2):328–333, 2009.

Neuroscience Consortium

Workgroup Keeps NIDA on the Cutting Edge of Brain Science

BY LORI WHITTEN,
NIDA Notes Staff Writer

The past 4 decades have witnessed explosive growth in knowledge about the brain's inner workings. For example, neuroscientists have identified an expanding list of neurochemicals and receptor proteins that form the backbone of cell-to-cell communication, developed animal models that mimic neurological conditions, and parsed how gene activation and suppression by environmental factors influence learn-

announce new tools and insights that have potential to reduce drug abuse and addiction and ameliorate their health and social consequences. It is the mission of the Institute's Neuroscience Consortium to monitor developments in brain science and ensure that NIDA's research programs are infused with the most current and most powerful knowledge and tools.

SHARING NEUROSCIENCE KNOWLEDGE

Neuroscience is progressing so rapidly that scientists find it challenging to stay abreast of advances in their own areas, let alone across the entire field. Created in 1994, NIDA's Neuroscience Consortium helps NIDA staff keep pace with cutting-edge brain science related to addiction. The

ing and memory. NIDA-funded scientists have contributed to and drawn upon these advances as they have established that drug addiction is a brain disease—the conceptual foundation of effective drug abuse treatment and prevention.

Today the rate of discovery in brain science is swifter than ever. Each week, neuroscience labs and journals

approximately 50 Consortium members represent every division of NIDA and virtually all offices, centers, and programs. Co-chairs of the Neuroscience Consortium—NIDA's Science Education Coordinator Dr. Cathrine Sasek, Office of Science Policy and Communications, and Program Officer Dr. Mary Kautz, Clinical Neuroscience Branch, Division of Clinical Neuroscience and

Behavioral Research—coordinate the group's overall activities. Other members initiate and lead activities according to their interests and expertise.

Consortium members seek out and share the latest, most promising findings with each other and the rest of the Institute staff. Part of each monthly Consortium meeting is devoted to what the group calls Hot Trends in NeuroScience. One member reports on a research paper relevant to his or her area. The group discusses the study, focusing on how the results might influence NIDA's research. Consortium members then share the information with other NIDA colleagues whose initiatives might benefit from it.

The Consortium also conducts NIDA's Cutting Edge Seminar series for all staff, other NIH researchers, and the public. These seminars enlist speakers from outside NIDA—some from other NIH institutes, others from universities—for a half-day event focusing on a specific topic. A 2009 Cutting Edge Seminar, for example, presented the techniques, findings, and potential of resting state functional connectivity. This promising new neuroimaging approach analyzes the network dynamics of the whole brain when a subject is awake but not responding to any particular external stimulus. The technique measures synchronous activity across brain regions. Researchers are investigating how resting brain dynamics differ between normal individuals and people with brain disorders, such as attention deficit hyperactivity disorder and bulimia. The technique also examines brain dynamics as people shift from the resting state to a task-oriented one. NIDA-funded scientists are examining whether normal brain activity during the shifts is disrupted in people addicted to drugs.

The Consortium also organizes activities to attract a greater number

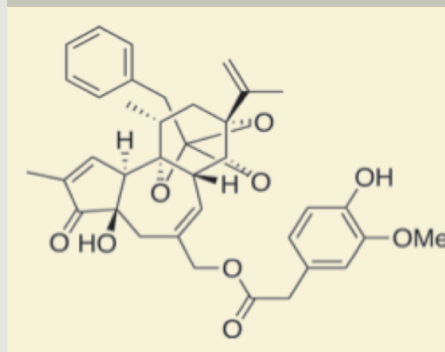


of talented scientists to the challenges of addiction research. As part of this effort, the Consortium coordinates a NIDA-sponsored Frontiers in Addiction Mini-Convention at the annual meeting of the Society for Neuroscience (SfN), the world's largest forum for research on brain science and health. The day-long mini-convention on trends in addiction research typically draws more than 500 scientists, including many who are new to addiction science. A highlight is always an address by the winner of the Jacob P. Waletzky Memorial Award, selected by SfN to recognize a junior scientist conducting innovative research into the neurobiology of drug addiction.

INFLUENCING NIDA PROGRAMS

Consortium activities have had a major impact on NIDA research programs and initiatives. For instance, in a November 2002 Cutting Edge Seminar, Dr. Andrew Mannes of the National Institute of Dental and Craniofacial Research presented his results from animal research on the pain-fighting effects of resiniferatoxin (RTX)—a naturally occurring nonopioid pain reliever with a different biological target than most analgesics (“Basic Science Discoveries Yield Novel Approaches to Analgesia,”

FROM PLANT TO PAINKILLER The Use of Resiniferatoxin to Reduce Chronic Pain by Selectively Ablating Spinal C-Fiber, a Cutting Edge Seminar sponsored by the Neuroscience Consortium, called NIDA program officers' attention to research on resiniferatoxin (RTX; below, left). That chemical had been extracted from a cactus-like plant, *Euphorbia resinifera* (below, right) and seems to provide powerful pain relief. NIDA subsequently facilitated FDA approval for clinical trials to be conducted by Dr. Andrew Mannes of the NIH Clinical Center. Because RTX does not act on brain receptors, it may offer a long-term treatment for some types of chronic pain without many of the side effects and addiction potential that are associated with opioid analgesics.



NIDA Notes, Volume 22, Number 1, page 1). NIDA staff who coordinate efforts to develop safe and effective treatments for pain attended the seminar and subsequently formed a team to seek approval from the Food and Drug Administration (FDA) for clinical trials of RTX. In 2008, the FDA granted such approval for the testing of RTX in patients with pain from advanced cancer. Initial findings indicate that RTX has strong analgesic power with no appreciable side effects.

“The pace of new findings in neuroscience is staggering, and it is necessary

to learn from each other to keep up,” says Dr. Kautz. “As a program official, I find Consortium events thought-provoking and a great opportunity to find out about advances in neuroscience. These help NIDA staff to generate creative approaches to the science of addiction.”

Looking to the future, the Consortium plans to continue to highlight exciting findings about the brain. “Our goal is to encourage NIDA scientists to delve into new areas of scientific inquiry that have great potential to transform addiction research,” says Dr. Sasek. ■

NIDAMED

NIDAMED: Resources for Patient Care

NIDAMED is a NIDA initiative designed to provide the medical community with drug abuse resources to enhance patient care.

At the heart of NIDAMED are research-based drug use screening tools and resources. Designed with the demands of modern clinical practice in mind, these products help clinicians to efficiently screen at-risk patients and conduct the followup steps necessary to provide excellent medical care.

Visit www.drugabuse.gov/NIDAMED for more information.



■ COCAINE VACCINE

[Continued from page 1]

drug typically in the body during cocaine abuse. The remaining 57 patients received placebo injections on an identical schedule. All patients also attended weekly drug abuse counseling sessions focused on relapse prevention. The participants submitted urine samples for cocaine assay three times each week and gave blood samples for antibody level monitoring at the end of the second week and then at 4-week intervals.

ANTIBODY LEVEL CRUCIAL

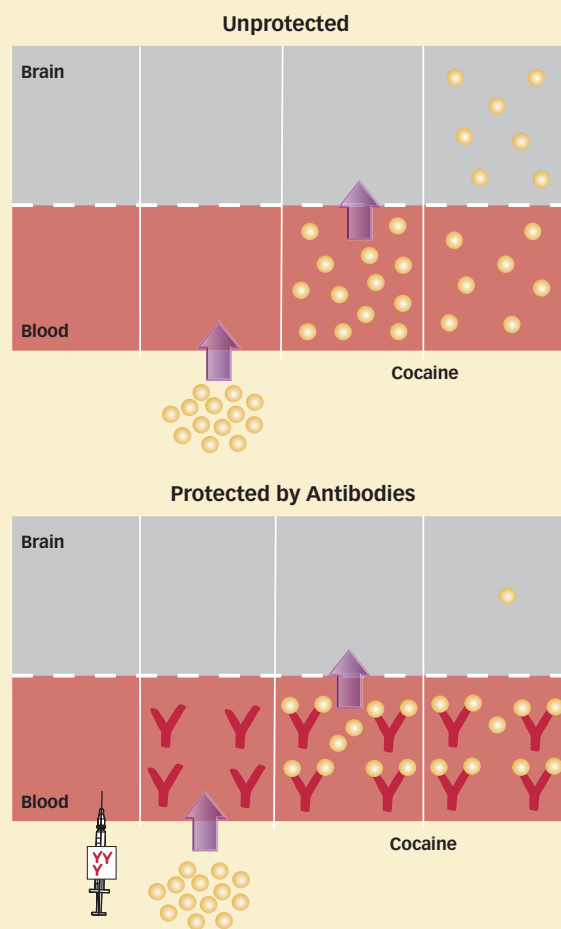
Some of the patients noted that the vaccine achieved its desired effect of suppressing cocaine's psychoactive effects. These individuals said that they felt little difference even after taking large amounts of the drug—in some cases up to 10 times their normal intake—confirmed by levels of a cocaine metabolite in their urine. In most of these cases, loss of cocaine's psychoactive effects occurred after three to four injections of the vaccine.

The patients who received the vaccine and those given placebo both reduced their cocaine use, but the former did so more rapidly. During the period of highest antibody response to the vaccine—from the week following the fourth booster injection through the month following the final one—30 percent of the vaccinated patients, but only 15 percent of the placebo patients, achieved a 50 percent reduction in cocaine-positive urine samples compared with levels at the beginning of the study. In prior research, this measure of success corresponded with improvements in daily functioning among people addicted to cocaine, Dr. Kosten says. No further injections were given after the 12th week of the study, and the difference in cocaine use between the vaccine and placebo groups disappeared by week 16.

The vaccinated patients varied greatly in their antibody responses, and only 38 percent of the 55 who completed the entire series of injections produced anti-cocaine antibodies in the quantity (at least 43 $\mu\text{g}/\text{mL}$ of blood) that the researchers calculate will reliably block drug-induced euphoria. During the 8 weeks of the greatest antibody response, this group provided cocaine-free urine samples 45 percent of the time, as compared with 35 percent for the placebo group and the group with a lesser response to the vaccine. Of the patients who produced euphoria-blocking antibody levels, 53 percent at least doubled the frequency with which their urine samples demonstrated no new cocaine use, compared with 23 percent of those who received the vaccine but produced lower levels of the antibodies.

"If a patient makes enough antibodies, this treatment works well," says Dr. Kosten. Among cocaine abusers who receive the full course of injections, those who are motivated to quit are expected to achieve abstinence with a lower level of antibody than those who are not motivated to quit, he adds. Dr. Kosten

VACCINE DESIGNED TO KEEP COCAINE OUT OF THE BRAIN Under normal conditions, cocaine molecules (shown as gold circles) easily cross from the blood into the brain (top diagram). A series of vaccines, however, stimulates patients' immune systems to produce cocaine antibodies (red Ys) that attach to molecules of the drug and prevent them from reaching the brain (bottom diagram).



estimates that, with the current vaccine, about 70 percent of cocaine abusers would develop high enough levels of antibody to block cocaine's euphoric effects by more than 90 percent, an effect considered sufficient to prevent relapse in individuals motivated to quit. However, people not motivated to quit but who receive the antibody treatment, perhaps in response to family pressure or other reasons, would require an antibody level high enough to completely prevent euphoric effects from whatever amount of cocaine they typically take.

There were no serious adverse events related to the vaccine, and no patients dropped out of the study because of the treatment. “The active protein components of this vaccine (cholera toxin B) and the adjuvant of aluminum are used widely; millions of people have received them,” says Dr. Kosten. “Because the amount of cocaine in this vaccine is very small, it poses no threat to safety.”

IMPROVING THE VACCINE

Dr. Kosten’s team is currently planning to enroll 300 participants in a large NIDA-supported multisite trial to confirm the results of this proof-of-concept study and determine whether the vaccine can benefit the general population of cocaine abusers. The team expects the challenge of retaining patients for the entire course of vaccinations and assessments to be greater than in the just-completed trial, however, as none will be opiate abusers

scheduled for daily clinic visits for methadone. To bolster participants’ motivation, the researchers are supplementing relapse-prevention behavioral therapy with the opportunity to earn rewards for keeping clinic appointments.

In other ongoing research with different collaborators, Dr. Kosten is modifying

There were no serious adverse events related to the vaccine, and no patients dropped out of the study because of the treatment.

the vaccine in hopes of producing a stronger, more sustained antibody response. The researchers have replaced the cholera toxin with a carrier molecule developed by Merck Pharmaceuticals from the *Neisseria meningitidis* bacteria coat protein, which has boosted the amount of antibodies produced by other vaccines. This car-

rier has been used in a human meningitis vaccine for over 10 years. The newly configured vaccine has reduced cocaine self-administration in animals but has yet to be tried in people.

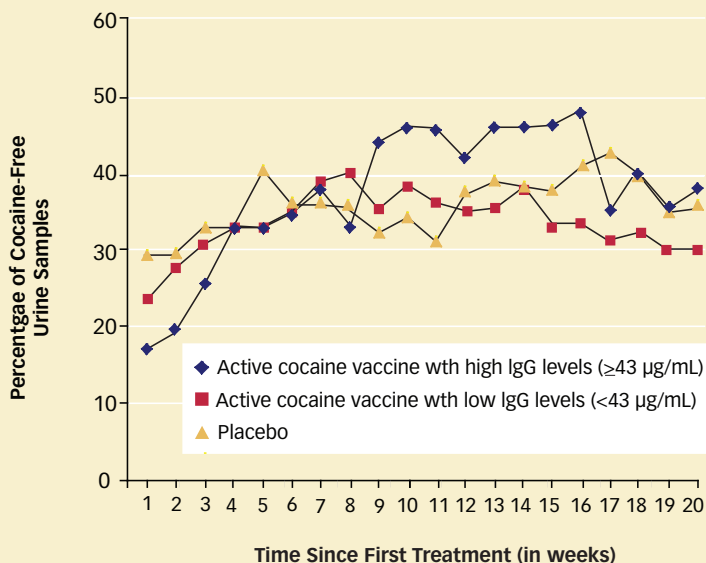
Dr. Kosten envisions a 2-year course of vaccine-aided therapy for cocaine addiction that will include behavioral therapy

and a series of vaccine injections followed by bimonthly or quarterly boosters.

Dr. Jamie Biswas of NIDA’s Division of Pharmacotherapies and Medical Consequences of Drug Abuse agrees with this proposed length of treatment: “Patients need a couple of years of blocking the cocaine high to get used to being off the drug, and they may benefit from appropriate behavioral therapies as well.

“NIDA is interested in vaccines as a therapeutic strategy for mopping up an abused drug before it reaches the brain, as an alternative to addiction medications that influence the nervous system directly,” Dr. Biswas adds. In addition to the cocaine vaccine, NIDA’s immunotherapy program supports the development and testing of vaccines for smoking cessation and to counter overdoses of phenylcyclidine (PCP), methamphetamine, and amphetamine (see “Antibody Fragment Removes Methamphetamine From the Brain,” *NIDA Notes*, Volume 22, Number 5, page 6).

ANTIBODIES HELP CUT COCAINE ABUSE As the study progressed from week 1 to week 16, all patients reduced cocaine abuse—but vaccine recipients did so more quickly and to a greater extent. During the vaccination period, those who produced high levels of cocaine-blocking immunoglobulin G (IgG) antibodies (greater than or equal to 43 µg/mL) submitted a greater percentage of cocaine-free urine samples than participants who had a lesser response to the vaccine or those in the placebo group.



SOURCE

Martell, B.A., et al. Cocaine vaccine for the treatment of cocaine dependence in methadone-maintained patients: A randomized double-blind placebo-controlled efficacy trial. *Archives of General Psychiatry* 66(10):1116–1123, 2009.

Study Supports Methadone Maintenance in Therapeutic Communities

Methadone-treated and other patients fare equally well.

BY LAURA BONETTA,
NIDA Notes Contributing Writer

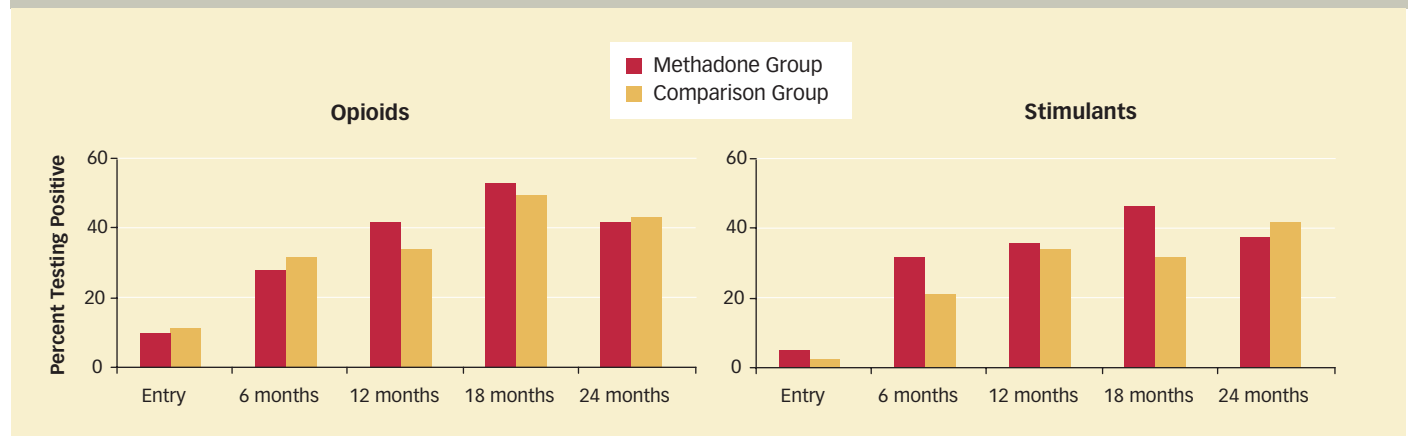
Methadone maintenance and therapeutic communities are two effective treatment approaches that are seldom combined. Few methadone patients apply to therapeutic com-

undermine other members' unity of purpose, threatening their progress. Practical and logistical difficulties add to the challenge of merging the two treatments.

In a recent NIDA-funded study, Dr. James Sorensen and colleagues at the University of California, San Francisco, showed that these issues, although significant, need not be prohibitive.

peutic community that has been accommodating methadone patients for over 2 decades. All the participants were opioid-dependent and met eligibility criteria for methadone maintenance therapy, and roughly half were receiving methadone. The methadone patients were similar to the others in terms of co-occurring stimulant abuse, psychiatric history, criminal

METHADONE PATIENTS FARE AS WELL AS DRUG-FREE PATIENTS IN A THERAPEUTIC COMMUNITY SETTING At half-yearly assessments, the proportions of methadone and comparison-group patients testing positive for illicit opioid or stimulant use were statistically equivalent. In both groups, the number of individuals using opioids or stimulants increased as more people left the treatment program. All study participants were tracked for 2 years whether or not they left treatment; participants who switched into methadone treatment during the study are included among the comparison group in this graph.



munities, and few therapeutic communities will accept them. Methadone patients may anticipate that therapeutic communities will be inhospitable because many therapeutic communities traditionally have held that recovery requires abstinence from all psychoactive drugs, including medications. Therapeutic communities may be concerned that admitting methadone-reliant individuals could

Opioid-dependent patients who were taking methadone upon admission to a therapeutic community fared as well as the rest of the community over 2 years of followup.

EQUIVALENT RESULTS

The researchers recruited 145 men and 86 women at the time of their admission to Walden House, a San Francisco thera-

justice involvement, and expected length of stay in the therapeutic community.

At the beginning of the study and then at 6, 12, 18, and 24 months, the researchers tested participants for use of illicit opioids, alcohol, and stimulants (cocaine and amphetamine) and questioned them about drug injection and risky sexual behaviors. They used the program's client database and staff logs to determine par-

Many Patients Still Receive Lower Than Recommended Methadone Doses

Methadone is a synthetic agent that relieves symptoms of withdrawal from heroin and other opioids by occupying the same brain receptor as those drugs. This therapy has been shown to have many benefits, including reductions in illicit drug use, needle-associated diseases, and crime. The treatment can also help a person work and participate in other normal social interactions.

In the United States, there are about 1,400 methadone maintenance programs serving over 254,000 patients, according to a 2006 report by the Substance Abuse and Mental Health Services Administration. Research has established that most patients require a methadone dose of 60–120 mg/day, depending on their individual responses, to achieve optimum therapeutic effects. Yet, a study by Drs. Harold Pollack and Thomas D’Aunno at the University of Chicago found that many methadone patients receive lesser doses.

In 1988, 1990, and then at 5-year intervals through 2005, the researchers surveyed nationally representative samples of 146 to 172 outpatient treatment facilities. Although the proportion of patients receiving doses below the recommended minimum decreased during this 17-year span, 34 percent of patients in 2005 still received methadone doses of less than 60 mg/day, while 17 percent received doses below 40 mg/day. The study also found that methadone programs strongly advocating an abstinence recovery goal were the most likely to provide doses of methadone below 60 mg/day.

SOURCE

Pollack, H.A., and D’Aunno, T. Dosage patterns in methadone treatment: Results from a national survey, 1988-2005. *Health Services Research* 43 (6): 2143–2163, 2008.

ticipants’ retention in treatment. Previous studies had indicated that the longer patients stay in treatment, the greater their likelihood of recovery.

By all measured outcomes, the methadone patients were statistically indistinguishable from patients who were not receiving that medication. In particular, both groups of patients stayed in treatment for similar periods of time and had similar success rates in avoiding illicit opioids and stimulants (see graph, page 8).

“The methadone patients’ outcomes were entirely equivalent to those of other patients,” says Dr. Sorensen. “That removes one reason for not admitting them to therapeutic communities.”

NECESSARY ADJUSTMENTS

During the past decade, some therapeutic communities have modified their programs to be accessible to a broader

range of patients, such as those with psychiatric disorders. Some of these individuals receive medications to treat their conditions, “but methadone still remains an issue,” says Dr. Sorensen.

A 2005 national survey of 380 therapeutic communities by the Institute for Behavioral Research at Texas Christian University found that only 7 percent of therapeutic communities integrated methadone treatment into their programs. A more recent survey by the Substance Abuse and Mental Health Services Administration determined that among residential treatment settings, including halfway houses and therapeutic communities, only 3.6 percent used methadone in their opioid-treatment programs.

Therapeutic communities wishing to integrate methadone patients into their programs must teach staff and their other

patients to understand the medication’s effects and counter negative attitudes toward it, says Dr. Sorensen. “There has to be training about what it is like to be on methadone and how to work with individuals who are taking it. A program needs to provide staff with strategies that they can use in working with issues specific to patients who take methadone, such as being drowsy and falling asleep at meetings.” He notes that similar problems arise with other psychiatric medications.

There also are practical hurdles, such as difficulty in supplying the medication. In the United States, methadone is typically provided in highly regulated clinics that patients initially have to visit each day to receive their dose; only after several months of adherence to the clinic’s regulations are patients allowed to take home a supply of methadone. Unsupervised trips to a methadone clinic may expose

therapeutic community patients to risks such as encounters with drug dealers or old acquaintances who are still abusing drugs. Thus, a residential facility accepting methadone patients needs to provide transportation to and from the clinics, as well as a secure place for storing and administering the medication.

All these provisions require additional staff and resources, and thus add costs. Yet for therapeutic communities that make the investment, the payoff is the capacity to provide more patients with the benefits of the therapeutic community model: a safe place to interact with peers who share experiences, an emphasis on self-reliance, a program of motivational reinforcement, and a dedication to recovery.

Dr. Sorensen and colleagues note that therapeutic communities that adjust to accommodate methadone patients give residents a useful treatment option. At

the 2-year mark of the study, a significant number—about 30 percent—of the individuals who started their residencies in the drug-free group had initiated methadone maintenance therapy. Methadone maintenance patients, in contrast, tended to continue with their original therapy.

“It is not a trivial matter to incorporate methadone treatment in a residential treatment setting, but we encourage therapeutic communities to do so,” says Dr. Sorensen. “In that way, they can expand the care they are providing to reach more patients.”

“Dr. Sorensen has shown that therapeutic communities can support the recovery of patients regardless of whether their therapeutic goals are abstinence or long-term maintenance,” says Dr. Thomas F. Hilton of NIDA’s Health Services Research Program.

Partly because of Dr. Sorensen’s work, there is now a growing openness toward the integration of different medical treatment approaches within therapeutic communities, including addiction pharmacotherapies. “Dr. Sorensen’s research is helping therapeutic communities evolve so that they can reach a broader spectrum of patient recovery needs,” Dr. Hilton adds. ■

SOURCES

Chen, T., et al. Residential treatment modifications: Adjunctive services to accommodate clients on methadone. *American Journal of Drug and Alcohol Abuse* 35(2):91–94, 2009.

Hettema, J.E., and Sorensen, J.L. Access to care for methadone maintenance patients in the United States. *International Journal of Mental Health and Addiction* 7(3):468–474, 2009.

Sorensen, J.L., et al. Methadone patients in the therapeutic community: A test of equivalency. *Drug and Alcohol Dependence* 100(1–2):100–106, 2009.

NIDA at Your Fingertips

www.drugabuse.gov

News and information about NIDA research, programs, and events are quickly and easily accessible through NIDA’s home page:

The screenshot shows the NIDA website home page with a navigation bar at the top containing links for HOME, ABOUT NIDA, NEWS, MEETINGS & EVENTS, FUNDING, PUBLICATIONS, MEDICAL & HEALTH PROFESSIONALS, RESEARCHERS, TEACHERS & YOUNG ADULTS, and SPANISH. Below the navigation bar, there are several featured sections: 'FRONTIERS' with a link to the 2010 Mini-Convention of the Society for Neuroscience; 'DRUG FACTS CHAT DAY' for November 9, 2010; 'Avant-Garde Award' for 2011; 'Students & Young Adults' section with links to drug information, education materials, and curriculum guides; 'Parents & Teachers' section with links to drug information and classroom tools; 'Medical & Health Professionals' section with links to NIDAED screening tools and resources; 'Researchers' section with links to grants and funding; 'Meetings & Events' section with links to upcoming meetings; 'Clinical Trials Information' section with links to clinicaltrials.gov and NIDA's Clinical Trials Network; 'En Español' section with links to resources in Spanish; and 'Publications Catalog' section with a link to view and order publications.

- Information on Drugs of Abuse
- Publications (including *NIDA Notes*)
- Calendar of Events
- Links to NIDA Organizational Units
- Funding Information
- Internal Activities
- Links to Related Web Sites

Marijuana Linked With Testicular Cancer

Use is associated with more aggressive form of the disease.

BY LORI WHITTEN,
NIDA Notes Staff Writer

Men who use marijuana may increase their risk for developing testicular cancer. A recent study of several hundred Washington State men with testicular cancer showed an association between current marijuana use and the more aggressive of the two types of the disease. Moreover, the association was strongest among men with a long history of regular marijuana use.

To firmly link marijuana use and the cancer, however, scientists will need to replicate the findings among large groups of men across many geographical regions and identify the underlying biological mechanisms, says NIDA-funded researcher Dr. S. K. Dey of the Cincinnati Children's Hospital Medical Center, who collaborated on the study with Drs. Janet Daling and Stephen M. Schwartz and colleagues at the Fred Hutchinson Cancer Research Center and the University of Washington.

During the past 50 years, the number of new cases of testicular cancer reported annually in the United States has nearly doubled. So has the percentage of the general population who report having smoked marijuana at least once. Dr. Dey suspected that the two trends might be related, although exposure to various environmental factors may also be involved.

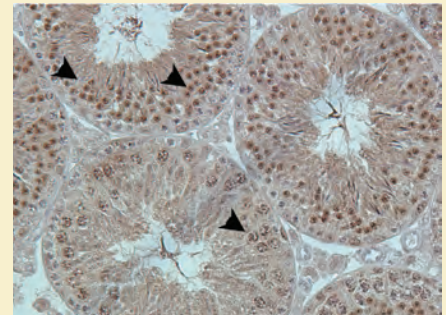
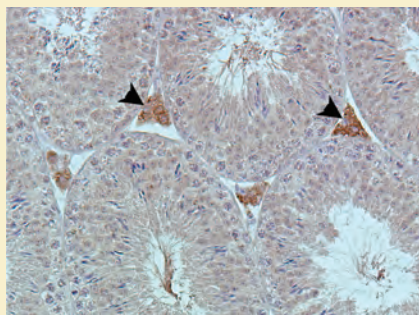
Along with the simultaneous rise in rates, there are biological reasons to

hypothesize a connection between the drug and the cancer. Research has shown that marijuana smoking reduces sperm production and male fertility, and other work has linked diminished fertility to increased risk of testicular cancer. Cannabinoid receptors—the cell-membrane proteins that bind to a component of mar-

recruited all of the study participants from three counties in Washington State and controlled statistically for smoking, drinking, and other testicular cancer risk factors.

Approximately 70 percent of each group reported smoking marijuana at least once. The researchers found that the

STRUCTURAL CONNECTION? Cannabinoid receptors (at arrows) of two types, cannabinoid 1 receptors (left) and cannabinoid 2 receptors (right), occur in mice testes cells (shown). Human testes cells also have these receptors. These proteins may underlie a proposed link between marijuana smoking and testicular cancer.



Biology of Reproduction 80(2):235–242, 2009.

ijuana as well as to the naturally occurring compounds known as endocannabinoids—occur on the cell membranes of sperm, the testes (see photograph), the uterus, and embryos, as well as on brain neurons. Marijuana smoking causes widespread effects in the endocrine and reproductive systems and might alter the growth of somatic and germ cells in the testes, resulting in testicular cancer.

The research team interviewed 369 men who were diagnosed with testicular cancer between 1999 and 2006 and 979 men who never had the disease. They

odds of having testicular cancer were 70 percent higher among men who reported current marijuana use compared with nonusers. In addition, the researchers observed 80 percent higher odds of testicular cancer among men who started to use marijuana before age 18 compared with nonusers. They also found that the odds for testicular cancer among men who used marijuana at least weekly were twice that of nonusers.

Of the two categories of testicular cancer, nonseminomas and seminomas, the former was strongly associated with

a history of marijuana smoking, but the latter had little or no association, Dr. Dey says. Nonseminomas occur in younger men, grow more rapidly, and have lower survival rates. While a man diagnosed with seminomas is 98 percent as likely as someone without the disease to still be alive 10 years later, the figure for someone diagnosed with a nonseminoma ranges from 46 percent to 92 percent, depending on the tumor subtype. (For more information on these cancers, see http://seer.cancer.gov/publications/survival/surv_testis.pdf.)

The association between marijuana smoking and nonseminomas, but not seminomas, is difficult to explain, says Dr. Dey. The rates for both types of cancer have been rising, and subnormal fertility and certain environmental exposures

during puberty—such as chemicals that affect estrogen and androgen production—are risk factors for both.

“My colleagues and I hope our study sparks similar epidemiological investigations of the relationship between testicular cancer and marijuana abuse around the world,” says Dr. Dey. “These results may also spur animal research, which is essential for interpreting our findings.”

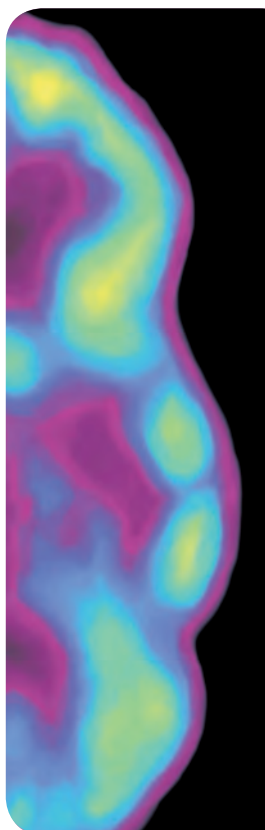
Animal research, he says, will be required to determine whether marijuana’s psychoactive ingredient, delta-9-tetrahydrocannabinol (THC), or its other components increase the risk of testicular cancer. Studies with animals may also search for molecular pathways connecting marijuana and testicular cancer. Such studies would probably focus on marijuana’s activation of the neurotransmit-

ter system that underlies its psychoactive, endocrine, and reproductive effects.

“If these interesting findings are replicated in a large, nationally representative group of participants, then future research should delve into the molecular mechanism underlying the association,” says Dr. Vishnudutt Purohit of NIDA’s Division of Basic Neuroscience and Behavioral Research. He notes that the study by Drs. Dey, Daling, and Schwartz is part of NIDA-supported research to determine how drugs of abuse affect the cardiovascular, pulmonary, reproductive, and immune systems of the body. ■

SOURCE

Daling, J.R., et al. Association of marijuana use and the incidence of testicular germ cell tumors. *Cancer* 115(6):1215–1223, 2009.



NIDA Center for Distributing Publications

Teachers, drug abuse counselors, parents, and others who want to order copies of NIDA’s publications have three quick-and-easy options:

- Call **1-877-NIDA-NIH**.
- Send an e-mail to **drugpubs@nida.nih.gov** specifying the name or catalog number of the publication and the mailing address to which it should be sent.
- Place an order at **www.drugabuse.gov/pubcat**. Visitors to the site can also peruse NIDA’s online catalog and read and download publications.



Multidimensional Family Therapy for Adolescent Drug Abuse Offers Broad, Lasting Benefits

An approach that integrates individual, family, and community interventions outperformed other treatments.

BY CARL SHERMAN,
NIDA Notes Contributing Writer

A therapy that engages substance abusing teens and their parents individually while building the relationship between them has lasting benefits that extend beyond reduced drug use, according to two NIDA-sponsored, randomized trials. A year after treatment, teenage participants treated with Multidimensional Family Therapy (MDFT) had fewer drug-related problems and had improved more on general measures of behavior and mental health than teens treated with cognitive-behavioral therapy (CBT).

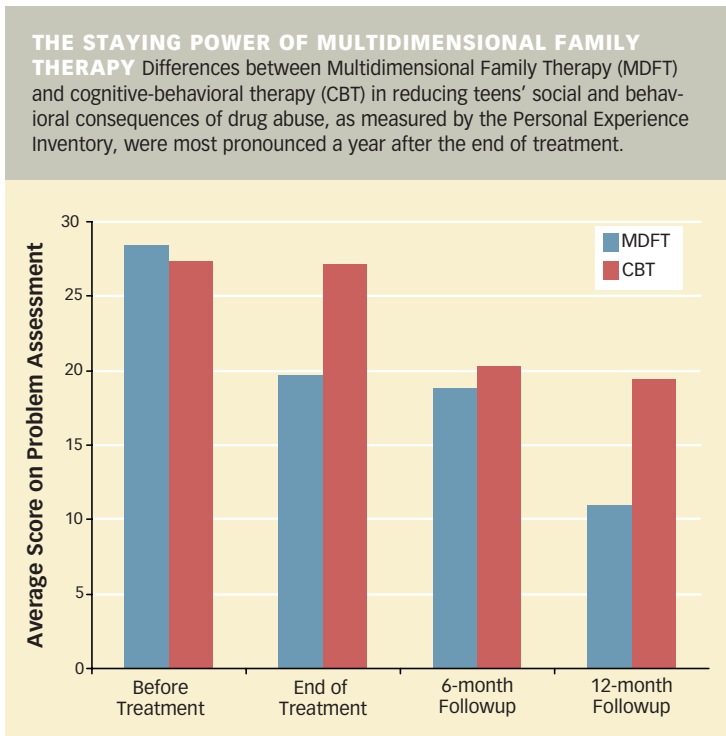
TEENS AND PARENTS, ALONE AND TOGETHER

In MDFT, adolescent drug abuse is viewed as a complex phenomenon in which personal issues, interpersonal relationships, overall family functioning, and social forces must all be addressed to effect enduring change. Some MDFT sessions involve both generations, some only the adolescent, and some just the parent or parents. In joint sessions, the therapist guides parents and teens through discussions of family problems and introduces methods that build family strengths, improve communication, and reduce conflict. Counselors also help families negotiate school, work, justice systems, and community service agencies.

Sessions held exclusively with individual teens aim to establish meaningful therapeutic goals, foster motivation, and help the adolescents develop concrete strategies to solve problems and find alternatives to drug taking and delinquency.

Sessions with parents include such topics as family management, the parent-adolescent relationship, and parenting skills, including monitoring and setting limits. These sessions also provide opportunities to provide emotional support. “We connect with parents in a way that recognizes their stress and the anger, hopelessness, and even despair they may feel about their child,” notes Dr. Howard Liddle of the University of Miami, who led the two studies. “Then we help parents reconnect emotionally to their child. This renewed caring is instrumental in changing parenting practices.

“MDFT is a flexible and individualized treatment system rather than a one-size-



fits-all approach,” says Dr. Liddle. MDFT has been used for young (11 to 15 years old) and older adolescents and juvenile offenders. It has been applied in clients’ homes, community-based clinics, residential treatment centers, and correctional facilities.

ADVANTAGES EMERGE OVER TIME

The setting for the first of the two studies was a community-based drug abuse clinic. Two hundred and twenty-four youths—predominantly African-American males, averaging 15 years of age, from low-income, single-parent homes—

participated. Cannabis was the most commonly abused drug; 75 percent of participants were diagnosed as cannabis dependent, 20 percent alcohol dependent, and 13 percent dependent on other substances. The researchers randomly assigned half to receive MDFT and half, CBT.

The CBT intervention, like MDFT, aimed to equip patients with skills not only to reduce drug abuse but also to cope with problems in many areas of life. However, unlike MDFT, it focused on individual, rather than family, development. Parents attended only the first two sessions, during which they helped their children assess their problems and prioritize goals. To ensure high-quality delivery of both interventions, counselors trained extensively with manuals, and research assistants rated videotapes of the therapy sessions.

“CBT is an evidence-based treatment that everybody knows about and likes, for good reason,” Dr. Liddle says. He notes that the empirical evidence supporting CBT for adults is strong and that similar evidence is emerging for adolescent populations as well. “Clinicians find it intuitive, logical, and if they have proper training, easy to do,” he explains.

At the conclusion of therapy in Dr. Liddle’s trial, CBT and MDFT seemed similarly effective. Youths in the CBT group reported that they had used cannabis 10 times, on average, in the month before they started treatment; those in the MDFT group reported 12 days of such usage. By the last month of treatment, both groups’ use of cannabis had dropped, to 7.5 days and 6 days, respectively. A similar pattern held for use of any drugs or alcohol. At intake, 94 percent of the CBT group and 92 percent of the MDFT youths reported using drugs or alcohol more than once in the previous month; these percentages had dropped to 77 and 73 percent, respectively, at discharge.

In the months after treatment, youths who had received MDFT fared better than those in the CBT group. Using a statistical technique called latent growth curve modeling, which compares rates of change over time, the researchers concluded that by 6 months after the start of treatment, the benefits of MDFT had begun to outpace those of CBT. One year after starting treatment:

- Youths assigned to MDFT had lower scores on the Personal Experience Inventory, which assesses impairment due to personal, social, educational, and legal problems tied to drug abuse.
- MDFT recipients were using drugs other than cannabis less frequently than before treatment, while such drug use by CBT recipients increased over pre-treatment levels.
- 47 percent of youth treated with MDFT had used alcohol or drugs no more than once in the prior month, compared with 28 percent in the CBT group.

MDFT ALSO BENEFITS YOUNGER TEENS

The second study tested MDFT versus CBT-based peer-group therapy in a younger group of adolescent substance abusers—a population that is at particularly high risk of worsening developmental problems, severe and chronic substance use disorders, depression, school failure, and unemployment in adulthood. Eighty-three teens, average age 13.5 years old, participated. Most had been referred to a substance abuse treatment program by either their schools or the juvenile justice system after using alcohol or a drug during the 30 days prior to an initial assessment or demonstrating imminent risk for substance use—for example, by getting caught with drugs in their possession.

As in the study with older youths, MDFT therapists counseled families as well as teens, but those conducting the

alternate therapy did not work at all with families. Both treatments lasted 12–16 weeks and addressed substance abuse together with associated problems, such as low self-esteem and school and social difficulties.

As in the earlier study, both treatments were effective at discharge, but once again MDFT recipients experienced longer lasting gains. At a followup assessment 12 months after the adolescents started treatment, only 7 percent of the MDFT sample reported substance use in the previous 30 days, compared with 45 percent of youths who had received the CBT-based group therapy. Remarkably, the MDFT recipients’ prevalence of drug use at this juncture also compared favorably with the rate of 8.5 percent reported by a nationally representative sample of eighth graders in the Monitoring the Future study.

In addition, during the followup year, MDFT recipients:

- improved their academic performance, while the grades of youths who had had the CBT-based group therapy worsened;
- had fewer arrests and placements on probation;
- suffered fewer psychiatric symptoms, such as those related to depression and anxiety;
- reduced self-reported delinquency and associations with delinquent peers, while youths receiving the group CBT increased delinquent peer involvement.

“Consistent with results from our other trials, outcomes of MDFT appeared to improve even after therapists completed their work with teens and families,” Dr. Liddle says.

The young teens demonstrated another MDFT benefit: Participants were more likely to remain in treatment—an important challenge in substance use interventions. In the MDFT group, 97 percent of the participants completed treatment,

Therapy Powers HIV/STD Risk Reduction

In addition to reducing drug use, Multidimensional Family Therapy (MDFT) may also ameliorate a serious associated problem: behaviors that increase risk of human immunodeficiency virus (HIV) infection and other sexually transmitted diseases (STD). Interim data from a trial sponsored by NIDA's Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS) program support that suggestion. Participants were recently released juvenile offenders who were abusing drugs, a population in which risky sexual behaviors, such as unprotected sex, are especially widespread.

In the trial, 154 adolescents were randomly assigned to receive MDFT or usual services. While in detention, adolescents in both treatment groups had received a standard educational, one-session Centers for Disease Control HIV/STD risk-reduction program. After release and 1 to 2 months of therapy, adolescents in the MDFT group and their parents participated in three 2-hour multifamily group sessions designed to raise awareness of HIV/STD risks and encourage behavior changes to reduce them.

Data collected 6 and 9 months after release from detention were "generally promising," Dr. Liddle says. Most impres-

sively, according to Dr. Liddle, the rate of new infections declined over this period in the MDFT group. The researchers plan to track the teens for 42 months.

Dr. Liddle speculates that to the extent the intervention proves effective, it will reflect the power of family involvement. "Attending to and reducing high-risk sexual behavior is framed in the same way we approach adolescent drug taking," he says.

Dr. Akiva Liberman, formerly of NIDA's Division of Epidemiology, Services and Prevention, describes MDFT as "very relevant and appropriate for adolescents involved in juvenile justice. These youths face an array of problems—individual, social, and family. MDFT seems to be a natural fit."

SOURCES

Liddle, H.A., et al. Implementation Outcomes of Multidimensional Family Therapy-Detention to Community (DTC)—A Reintegration Program for Drug-Using Juvenile Detainees. *International Journal of Offender Therapy and Comparative Criminology*. Published online before print April 28, 2010, doi: 10.1177/0306624X10366960.

Marvel, F., et al. Multidimensional family therapy HIV/STD risk-reduction intervention: An integrative family-based model for drug-involved juvenile offenders. *Family Process* 48(1):69–84, 2009.

compared with 72 percent of those who had CBT-based group therapy. Dr. Liddle notes that these engagement rates are far superior to the average rate of only 27 percent among those who completed 90 days of standard outpatient treatment in the NIDA-sponsored Drug Abuse Treatment Outcome Study (DATOS), a national study of adolescent drug problems.

In both of Dr. Liddle's studies, MDFT was administered by therapists from community-based drug-treatment agencies. "This suggests that the approach may be readily generalized to a serve a broad population," says Dr. Liddle.

"MDFT treatment outcomes are among the best there are for adolescents," says Dr. Lisa Onken, chief of the Behavioral and Integrative Branch of NIDA's

Division of Neuroscience and Behavioral Research. "Not only does it work, but it joins the category of behavioral interventions whose effects seem to endure after treatment ends."

Sustainability of treatment effects, as indicated by 12-month outcomes, was "the most important finding" of the studies, she says. "This is important particularly for younger adolescents, who would be on a very negative developmental trajectory without effective treatment."

Dr. Onken would like to see further research to identify which aspects of MDFT make it effective. "This is a very complex treatment, and the more we can figure out the essential ingredients—what is critically important and what is of lesser importance—the better we will be able to

implement it in the community," she says.

Dr. Liddle notes his team and others have begun work along these lines. ■

SOURCES

Liddle, H.A. Treating adolescent substance abuse using Multidimensional Family Therapy. In J. Weisz and A. Kazdin (eds.). *Evidence-based Psychotherapies for Children and Adolescents* (2nd ed.), New York: Guilford Press, pp. 416–432, 2010.

Henderson, C.E., et al. Parenting practices as mediators of treatment effects in an early-intervention trial of Multidimensional Family Therapy. *American Journal of Drug and Alcohol Abuse*, 35: 220–226, 2009.

Liddle, H.A., et al. Multidimensional Family Therapy for young adolescent substance abuse: Twelve-month outcomes of a randomized controlled trial. *Journal of Consulting and Clinical Psychology* 77(1):12–25, 2009.

Liddle, H.A., et al. Treating adolescent drug abuse: A randomized trial comparing Multidimensional Family Therapy and cognitive behavior therapy. *Addiction* 103(10):1660–1670, 2008.

NIDA Appoints New Director of the Intramural Research Program



Antonello Bonci, M.D., one of the world's leading researchers in neuropsychopharmacology, has joined NIDA as scientific director of the Intramural Research Program (IRP) in Baltimore.

Dr. Bonci is known for the elegance and multidisciplinary breadth of his studies on the long-term effects of drug exposure on the brain. Dr. Bonci and colleagues were

the first to demonstrate that drugs of abuse, such as cocaine, modify the strength of the connections between neurons. This finding cast drug addiction in a new light—as a process of maladaptive learning.

“We think Dr. Bonci will bring tremendous strength to our already robust intramural research portfolio,” says NIDA Director Dr. Nora D. Volkow. “His impressive background as a superb neuroscientist with strong clinical training brings NIDA an exceptional investigator committed to translational science and will bring us closer to new and better medicines for the treatment of addiction.”

Prior to joining NIDA, Dr. Bonci was in the Department of Neurology at the University of California, San Francisco, where he held the Howard J. Weinberg Endowed Chair in Addiction Research. In 2009, he received the Daniel H. Efron Award for outstanding basic and translational research at the American College of Neuropsychopharmacology. He also received the 2004 Jacob P. Waletzky Memorial Award, given to young scientists for innovative research in drug addiction and alcoholism.

“I am thrilled to be a part of one of the world's most important scientific organizations looking at the challenging problem of drug abuse and addiction,” says Dr. Bonci. “I especially look forward to working with Dr. Volkow and her colleagues in the extramural program, as well as the many top-level investigators at the IRP who have been responsible for many advances in addiction science.”

Dr. Bonci replaces Dr. Barry Hoffer, who had served as the IRP scientific director since 1996.

Addiction Science Award Winners Announced

NIDA presented Addiction Science Awards to three high school students during the 2010 Intel International Science and Engineering Fair (ISEF), held last May in San Jose, California.

Ameya Ashish Deshmukh, a 16-year-old student at Upper Arlington (Ohio) High School, won first place for his project, titled “Rational Drug Design Methods for the Identification of a Novel Negative Allosteric Modulator of $\alpha_4\beta_2$ Nicotinic Receptors.” To identify molecules that bind to nicotine receptors and thus demonstrate potential for treating nicotine addiction, he used computerized molecular models to compare candidate compounds identified by previous research and tested the finalists on human cells.

Second place went to Kevin Michael Knight, a 17-year-old student at Collegiate High School at Northwest Florida State College in Niceville, Florida. The results of his project, “Improving ADHD Treatment: A Comparison of Stimulant Medication Treatment for Children with ADHD, Computerized Cognitive Training of Attention and Working Memory, and the Combination of the Two,” suggest that some cognitive games could be useful, as an adjunct to medication, in treating attention deficit hyperactivity disorder.

Joseph Hunter Yagoda, a 17-year-old student at the William A. Shine Great Neck (N.Y.) High School, won third place for “Risky Business: What Cognitive Factors Influence Risk Taking in the Academic Setting?” He investigated the calculations that go into a teenager's decision to cut classes.

Friends of NIDA, a coalition of individuals and groups that support NIDA's mission, awarded scholarships to the winners: \$2,500 for first place, \$1,500 for second place, and \$1,000 for third place.



Addiction Science Award winners, Kevin Knight (2nd place), Ameya Deshmukh (1st place), Joseph Yagoda (3rd place).

Program Enhances Physician Knowledge on Substance Abuse

Although substance abuse can have significant health consequences, most medical schools do not provide future primary care physicians with adequate training on addiction. To address this situation, NIDA funded the development of the Chief Resident Immersion Training (CRIT) program in addiction medicine, which started in 2002.

An evaluation of the CRIT program at the Boston University School of Medicine was recently conducted by Program Directors Drs. Jeffrey H. Samet and Daniel P. Alford and

colleagues. They evaluated 64 chief residents who had participated in the CRIT program from 2003 to 2005. The researchers found that CRIT improved knowledge, confidence, and preparedness to diagnose, manage, and teach about substance abuse.

CRIT program developers chose chief residents because these young physicians help teach medical students and residents and often go on to other leadership roles. During the 4-day program, participants received science-based resources and teaching tools on substance abuse and met with individuals in recovery. They learned teaching techniques and, working with faculty mentors, developed plans to share newly learned knowledge and skills about substance abuse with other staff at their home institutions.

When retested immediately after the program, participants achieved an average score of 78 on a multiple-choice exam covering addiction neurobiology, screening, referral options, pharmacotherapy, and relapse, compared with 67 at the start of the training. The program also had a longer-term impact: 6 months after the training, 97 percent of participants reported being either more or much more likely to incorporate information on substance abuse into teaching than before the training. All the participants had developed a teaching project related to substance abuse, and 86 percent reported that these had an impact on their residency program curriculum. For more information on the CRIT program, see <http://www.bumc.bu.edu/crit>.

SOURCE

Alford, D.P., et al. Promoting substance use education among generalist physicians: An evaluation of the Chief Resident Immersion Training (CRIT) program. *Journal of General Internal Medicine* 24(1):40-47, 2009.

NIDA Grantee Wins Prize for Genetics Web Sites

Dr. Louisa Stark, a NIDA science education grantee, has won the *Science Prize for Online Resources in Education* for developing two interactive Web sites on genetics, one of which includes a module on addiction.

The first site, <http://learn.genetics.utah.edu>, explains genetics in terms that students in grades 5 through 12 can easily understand. It covers 15 topics ranging from DNA to epigenetics. The site's module "The New Science of Addiction: Genetics and the Brain" (<http://learn.genetics.utah.edu/content/addiction>) has been used in addiction treatment in several countries.

The second site, <http://teach.genetics.utah.edu>, complements the Learn Genetics materials. It helps educators bring genetics alive in the classroom by providing them with tools and resources

to supplement their curricula. Among these tools are "print and go" lesson plans covering a broad range of topics, such as cloning, gene therapy, personalized medicine, and stem cells.

Web designer Mr. Kevin Pompei collaborated with Dr. Stark in designing the sites. Dr. Stark is director of the Genetic Science Learning Center at the University of Utah.

Three Scientists Join Advisory Council

Three scientists have joined NIDA's National Advisory Council on Drug Abuse. The new members, presented at the council's February meeting, are:

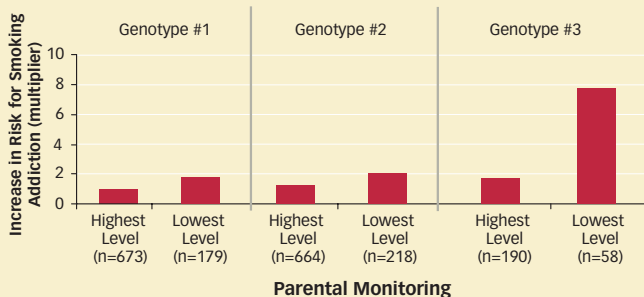
- **Caryn E. Lerman, Ph.D.**, a professor in the Department of Psychiatry and the Annenberg Public Policy Center and scientific director of the Abramson Cancer Center at the University of Pennsylvania. Dr. Lerman has extensive expertise in research on nicotine dependence, including behavioral pharmacology, pharmacogenetics, medications development, and, more recently, neuroimaging. She was recently elected president of the Society for Research on Nicotine and Tobacco.
- **Steven M. Wolinsky, M.D.**, a professor of medicine and chief of the Division of Infectious Diseases at Northwestern University's Feinberg School of Medicine. Dr. Wolinsky's research focuses on the evolutionary mechanisms underlying host-pathogen interactions and their role in the emergence, spread, and containment of infectious diseases, such as HIV/AIDS. He also considers how viral genetic variation, driven by host genetics and immunity, affects HIV infection dynamics and epidemic behavior.
- **Jon-Kar Zubieta, Ph.D., M.D.**, a research professor in the Molecular and Behavioral Neuroscience Institute, a professor in the departments of psychiatry and radiology, and director of the Neuroimaging Core at the University of Michigan. Dr. Zubieta's research focuses on the neurobiological mechanisms underlying the regulation of stress responses. He has extensive experience in the use of imaging technologies for the quantification of metabolism, blood flow, and neuroreceptor sites in human subjects. ■



NEW COUNCIL MEMBERS (From left) Drs. Caryn E. Lerman, Jon-Kar Zubieta, and (far right) Steven M. Wolinsky with NIDA Director Dr. Nora D. Volkow.

Parental Supervision and Genetics Interact To Influence Nicotine Addiction

GENE VARIANT AND LOW PARENTAL MONITORING COMBINE TO ELEVATE SMOKING RISK Increased risk of nicotine addiction conferred by one genotype of *CHRNA5* dramatically increases among people who experienced low parental supervision as young teens.



A gene variant that increases the risk for nicotine addiction exerts less influence when parents monitor young adolescents' whereabouts and activities, report Dr. Laura Jean Bierut and colleagues at Washington University in St. Louis and other institutions. They studied 2,027 adults who had smoked at least 100 cigarettes in their lifetime, of whom 1,032 were dependent on nicotine. The researchers determined which participants carried a specific variant of the gene called *CHRNA5*, which encodes the α_5 subunits of nicotinic acetylcholine receptors. The variant elevated the risk for smoking addiction eightfold among people who recalled lax parental supervision during their middle-school years, but it only doubled the risk among people who reported intense parental supervision. Among participants with two other genotypes of *CHRNA5*, low parental monitoring only roughly doubled risk for nicotine addiction.

In previous research, Dr. Bierut and colleagues had linked an increased risk for nicotine addiction to at least two distinct variants near the α_5 subunit of the nicotinic receptor (see "Studies Link Family of Genes to Nicotine Addiction," *NIDA Notes*, Volume 22, Number 6, page 1). The team's new research suggests that strong parental supervision may mitigate the influence of some addiction-associated genes by limiting young teens' opportunities to try cigarettes and to smoke regularly. Without these critical steps in the development of nicotine addiction, the genetic vulnerability never comes into play.

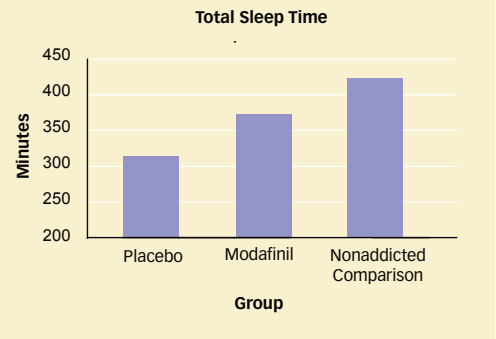
Addiction 104(10): 1731–1740, 2009.

Modafinil Normalizes Sleep During Early Cocaine Abstinence

Modafinil, a medication used to treat narcolepsy and related disorders, dramatically improves sleep among recently abstinent cocaine abusers. Better sleep may boost patients' attention, memory, and mood—helping them benefit from behavioral therapy for addiction.

Ten inpatients in a behavioral therapy program who received a daily morning dose of modafinil for the 16 days of the study fell asleep more quickly, spent more time in deep sleep, and slept longer than 10 inpatients in a placebo group, reports a team of NIDA-funded addiction and sleep researchers at the Yale and Harvard schools of medicine. All the inpatients were abstinent throughout the study, and the sleep of patients in the placebo group deteriorated during the weeks of abstinence. After 1 and 2 weeks of abstinence, patients treated with modafinil reported less daytime sleepiness and demonstrated less fatigue on tests than those who received placebo. On most measures, the sleep of the modafinil-treated cocaine abusers by the end of the study was more similar to that of 12 non-addicted volunteers than to that of the cocaine abusers receiving the placebo, reports the team, headed by Yale's Dr. Peter Morgan.

SLEEP OF ABSTINENT COCAINE ABUSERS NORMALIZES WITH MODAFINIL Cocaine abusers treated with modafinil for 16 days demonstrated improvements in several characteristics of sleep, including total sleep time.



The new results, the first to show modafinil's sleep-enhancing effects among abstinent drug abusers, extend the team's previous finding that during early abstinence, cocaine abusers demonstrate disrupted sleep without being aware of it ("Chronic Cocaine Abusers Have Occult Insomnia in Early Abstinence," *NIDA Notes*, Volume 21, Number 5, page 12). If the beneficial effects of modafinil are verified, clinicians may incorporate the medication into addiction treatment.

The new results, the first to show modafinil's sleep-enhancing effects among abstinent drug abusers, extend the team's previous finding that during early abstinence, cocaine abusers demonstrate disrupted sleep without being aware of it ("Chronic Cocaine Abusers Have Occult Insomnia in Early Abstinence," *NIDA Notes*, Volume 21, Number 5, page 12). If the beneficial effects of modafinil are verified, clinicians may incorporate the medication into addiction treatment.

American Journal of Psychiatry 167(3):331–340, 2010.

Drug Abuse at Highest Level in Nearly a Decade

Illicit drug use in the United States has risen to its highest level in 8 years, according to the 2009 National Survey on Drug Use and Health (NSDUH). Last year, 8.7 percent of Americans aged 12 and older—an estimated 21.8 million people—said they used illicit drugs in the month prior to the survey, which represents a 9 percent increase over the 2008 rate.

The rise was driven largely by an increase in the use of marijuana, which rose to 6.6 percent in 2009 after holding steady at around 6 percent since 2002. The increase was particularly high among youth aged 12 to 17 and young adults aged 18 to 25. Marijuana is the most commonly used illicit drug; about three-quarters of those who report illicit drug use cite marijuana abuse.

“These results are a wake-up call to the Nation,” said Ms. Pamela S. Hyde, administrator of the Substance Abuse and Mental Health Services Administration (SAMHSA), at a press conference held September 16 to announce the findings. “Our strategies of the past appear to have stalled with ‘Generation Next.’ Parents and caregivers, teachers, coaches, and faith and community leaders must find credible new ways to communicate with our youth about the dangers of substance abuse.”

Mr. Gil Kerlikowske, director of the White House Office of National Drug Control Policy, speculated at the press conference that daily coverage in the media of efforts to change state laws to allow the sale of “medical marijuana” and policy debates over legalization of the drug could be contributing to the notion that marijuana is benign.

Changes in state policies and the widening availability of medical marijuana are consistent with the shift in attitudes evident in the survey, says Dr. Wilson Compton, director of NIDA’s Division of Epidemiology, Services and Prevention Research. “However, we can’t tell which comes first,” he says. “Do the changes in perceived risk lead to changes in laws and regulations, or do these policy changes lead to a shift in attitudes?”

Dr. Compton says the rise in drug abuse also corresponds with a decrease in prevention messages targeting youth, as well as a weakening perception among young people that drugs are harmful. “We need to redouble our prevention efforts in families, schools, and communities,” he says.

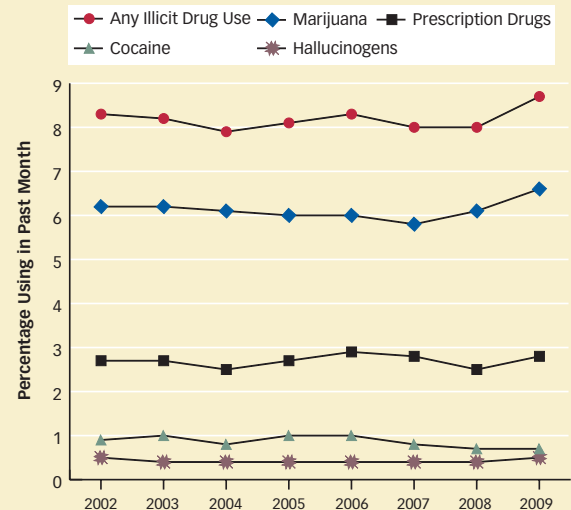
The increase in marijuana use was foreshadowed in survey results released late last year. Both the 2008 NSDUH survey and the 2009 NIDA-sponsored Monitoring the Future survey, which covers students in the 8th, 10th and 12th grades, indicated that

the decline in marijuana use over the past decade had begun to reverse. In the past few years, a growing percentage of youth who responded to the two surveys said they did not believe that regular use of the drug was very harmful.

PRESCRIPTIONS, METH, AND ECSTASY ON THE RISE

Abuse of prescription drugs and the less frequently used methamphetamine and ecstasy also saw increases. Nonmedical use of prescription drugs rose 12 percent, from 2.5 percent in 2008 to 2.8 percent in 2009. Abuse of methamphetamine rose from 0.1 percent to 0.2 percent, and ecstasy from 0.2 percent to 0.3 percent.

RISE IN MARIJUANA USE DRIVES UPSWING Marijuana is the most commonly used illicit drug, with 16.7 million people aged 12 and older reporting past-month use in 2009. A 6.6 percent increase in usage—the highest in 8 years—drove up overall illicit drug use.



The 2009 survey also found that:

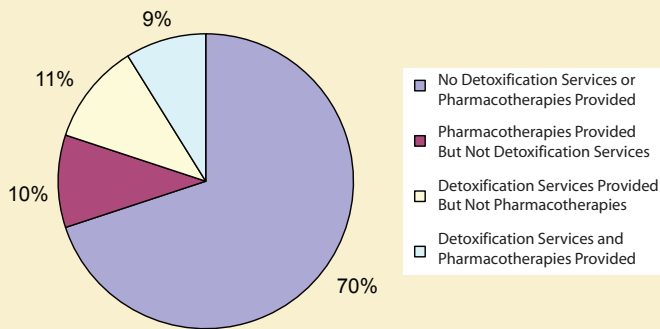
- Drug abuse among those aged 50 to 59 doubled to 6.2 percent from 2.7 percent in 2002. This trend reflects the entry into this age bracket of increasing numbers of baby boomers, who have a higher rate of illicit drug use than older cohorts.
- Only about 11 percent of those who need treatment for drug or alcohol abuse received therapy in a specialty facility. Previous years had shown a similar disparity.

The annual NSDUH survey is sponsored by SAMHSA. The 2009 results are based on responses from 68,700 civilians nationwide who do not live in institutions. The report is available online at www.oas.samhsa.gov/NSDUH/2k9NSDUH/2k9Results.htm. ■

SOURCE

Substance Abuse and Mental Health Services Administration, 2010. *Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings* (Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4586). Rockville, MD.

Detoxification Services and Pharmacotherapies Lacking in Nation's Jails and Prisons



Although many people in jails and prisons have a history of substance abuse, the majority of correctional facilities offer neither detoxification services to help inmates through drug withdrawal nor pharmacotherapies, such as methadone, naltrexone, or buprenorphine, to aid them in maintaining abstinence. The findings were derived from responses to a nationally representative sample of 198 correctional institutions that participated in the National Criminal Justice Treatment Practices survey, which was developed by NIDA's Criminal Justice-Drug Abuse Treatment Studies research network.

Source: Oser, C.B., et al. Organizational-level correlates of the provision of detoxification services and medication-based treatments for substance abuse in correctional institutions. *Drug and Alcohol Dependence* 103S:S73-S81, 2009.

NIDA Notes is a publication of the U.S. Government produced by the National Institute on Drug Abuse. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget. Except for material specifically identified as copyrighted, all materials appearing in *NIDA Notes* are in the public domain and may be reproduced without permission. Citation of the source is appreciated.

Subscriptions and Changes of Address

NIDA Notes Subscriptions Department:
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20852
Phone: 301-816-4614
Fax: 301-770-8205
E-mail: nidasubreq@rti.org

Additional Copies

DrugPubs Research Dissemination Center
Phone: 877-NIDA-NIH (877-643-2644)
TTY/TDD: 240-645-0228
Fax: 240-645-0227
E-mail: drugpubs@nida.nih.gov

NIH Publication No. 10-7443
Printed December 2010



OFFICIAL BUSINESS
Penalty for Private Use, \$300

ADDRESS SERVICE REQUESTED

National Institutes of Health
National Institute on Drug Abuse
6001 Executive Boulevard
Room 5213
Bethesda, MD 20892-9561



Presorted Standard
Postage and
Fees Paid
DHHS/NIH
Permit No. G-827