

A Special Supplement to NIDA's Bimonthly Newsletter *NIDA NOTES*



*National Institute on Drug Abuse*  
**25** *Years of Progress*  
*In Drug Abuse Research*

**National Institute on Drug Abuse: 25  
Years of Progress In Drug Abuse  
Research**

U.S. Department of Health and Human Services ■ National Institutes of Health

## *NIDA's Clinical Trials Network: A Partnership for the New Century*

**F**or real progress to be made in drug abuse treatment, research-tested approaches must be put into practice in the community settings where most treatment is provided. To speed that progress, during its 25th anniversary year NIDA has established the foundation for a nationwide partnership between treatment researchers and community-based treatment providers.

NIDA's new National Drug Abuse Treatment Clinical Trials Network will provide a structured partnership in which the Institute, treatment researchers, and community-based service providers will cooperatively develop, validate, refine, and deliver new treatment options to patients in community-level clinical practice.

The landmark Clinical Trials Network (CTN) will consist of Regional Research and Training Centers, each linked in partnership with 5 to 10 or more community-based treatment programs. This framework will provide a broad and powerful infrastructure for rapid multisite testing of promising science-based therapies. Thus, drug abuse patients across the country will benefit, and benefit sooner, from well-developed science-based care.

The size and diversity of patient populations participating in CTN studies will provide a resource for concurrent testing of promising therapies and will make it possible to conduct comprehensive investigations of factors such as environmental and genetic determinants of vulnerability to drug dependence and abuse.

The CTN partnership is designed to meet a range of objectives that include:

- integrating behavioral, pharmacological, and treatment research;
- supporting studies of behavioral, pharmacological, and combined behavioral and pharmacological treatment interventions in rigorous, multisite clinical trials;
- investigating the impact of advances in treatment research on community-level treatment practices;
- ensuring that treatment research in drug abuse and addiction meets the needs of the wider community, including minorities, women, children, and underserved populations;
- fostering the exchange of ideas, information, and values among community treatment practitioners and researchers; and
- determining the impact of effective treatments on the incidence and prevalence of other illnesses, such as HIV and hepatitis.

### *For More Information*

Additional information about the Clinical Trials Network is available through NIDA's home page on the World Wide Web at [www.nida.nih.gov](http://www.nida.nih.gov). ■■

# *NIDA at 25: A History of Accomplishment And a Vision of the Future*

By NIDA Director Dr. Alan I. Leshner

NIDA was established in 1974 to bring the power of science to bear on the Nation's drug abuse problems. The Institute's first 25 years have been marked by groundbreaking scientific discoveries about the nature of drug abuse and addiction and what to do about them. Together, these discoveries have established that addiction is a quintessential biobehavioral disorder—a brain disease with embedded behavioral and social aspects. This album commemorates the major milestones on NIDA's road of discovery.

At the time of NIDA's inception, many people incorrectly viewed drug addiction as simply a problem of people with character flaws and weak wills. Today, thanks to the research accomplishments of thousands of scientists, we have moved far beyond such simplistic ideologies to a better understanding of the complex biological, behavioral, social, and public health aspects of drug abuse. We now know that while initial experimentation with drugs may be voluntary, continuing drug use changes the brain in fundamental and long-lasting ways. These brain changes underlie the compulsive drug-seeking and drug-taking behaviors that are the hallmarks of drug addiction.

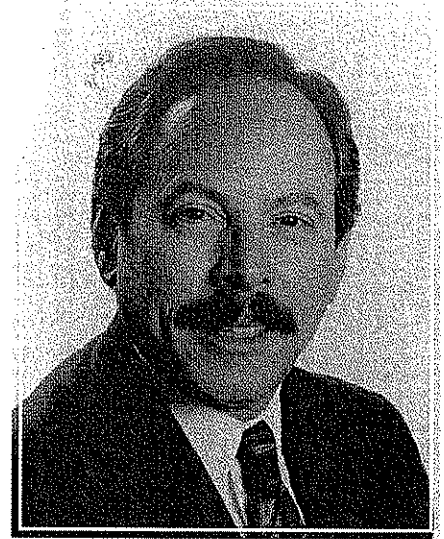
Over the last quarter century, biological and behavioral research conducted by NIDA's intramural and extramural scientists has clearly shown that drug abuse is a preventable behavior and drug addiction is a treatable disease. Based on this science, we have developed and implemented drug abuse prevention programs that can deter young people from drug abuse. We have developed a variety of behavioral and pharmacological treatments that can restore a high degree of normalcy to brain function and behaviors that have been disrupted by the addiction process. We have

learned that a comprehensive approach that combines behavioral and pharmacological treatment is the best way to treat the complex biological, behavioral, and social aspects of drug addiction.

And, we have convincingly demonstrated that appropriate medications and behavioral treatments reduce drug abuse, drug-related criminal behavior, and the harmful health and social consequences of drug abuse, such as HIV/AIDS.

To accelerate the pace of drug abuse research and its application to real-life settings, NIDA is establishing the National Drug Abuse Treatment Clinical Trials Network (CTN) throughout the United States. The CTN will revolutionize drug abuse treatment research, closing the gap that has existed for too long between treatment research and community practice. (For more on the CTN, see "A Partnership for the Next Century" on the opposite page.)

In the prevention area as well, NIDA is facilitating the integration of the latest research-based programs into existing State, county, and community systems. For example, county cooperative extension agents, operating under the U.S. Department of Agriculture Cooperative Research, Extension, and Economic Service, have a long history of delivering life skills programs and scientific information to people in rural and urban communities across the Nation. Now NIDA-funded research being conducted at the University of Iowa in Ames is examining whether a research-based family drug abuse prevention program can be provided effectively through this extensive national service delivery system. In another example, scientists at the Pennsylvania State



University in University Park are giving teachers the opportunity to modify a research-tested, school-based prevention program to suit individual teaching styles or classroom conditions.

NIDA is standing on the threshold of a new generation of drug abuse prevention research. Investigations to date have identified numerous factors that can increase a person's vulnerability to drug abuse, including biological responses to stress, lack of long-term goals, sexual abuse, and some mental illnesses. On the other hand, some life experiences appear to go far toward overcoming the impact of these vulnerability factors. For example, parental involvement in a child's life can lower the risk of drug abuse despite the presence of strong vulnerability factors. The next step will be to extend this knowledge and use it to design more sophisticated prevention programs with the flexibility to respond to community-specific needs. The CTN will facilitate this effort.

Technological advances have given researchers powerful tools that we can use to greatly amplify our understanding of the neurobiology of addiction. Positron emission tomography (PET), magnetic resonance imaging (MRI), and the newer magnetic resonance spectroscopy (MRS) have

permitted us to observe neuroanatomical changes due to prolonged drug use, information that was key to establishing addiction as a brain disease. In addition, NIDA scientists, using genetic engineering techniques,

have developed new animal models that can be used to obtain precise information about the neurochemical changes of addiction.

With these tools and others, NIDA will push basic research in two important new directions. First, to understand the disordered thinking processes asso-



*NIDA's forerunner, the United States Narcotic Farm, opened in 1935 as a unit of a U.S. Public Health Service hospital in Lexington, Kentucky.*

ciated with drug abuse, NIDA will promote research about drug effects in the areas of the brain that perform higher functions, such as planning and problem solving. Second, researchers will begin to trace the entire process of addiction—all the physiological changes leading from the first use of drugs to the development of craving and throughout the natural history of the disease. This research will inform and be informed by parallel studies of the progressive cognitive and behavioral changes associated with drug abuse and addiction. Ultimately, these studies will lead to medications and behavioral therapies that are appropriate for people in each stage of the continuum from initial drug use to established addiction and recovery.

Of course, while pursuing the next phases of treatment, prevention, and basic research, NIDA will continue to address the immediate challenges presented by drug abuse in the Nation. Currently, these include, most pressingly, the growing use of nicotine by young people, the spread of methamphetamine abuse to new populations and regions of the country, and the proliferation of club drugs.

In NIDA's first 25 years, the power of science has disproved ideologies, myths, and superstitions about drug abuse and addiction; improved the lives of drug abuse patients; and reduced the harmful individual, social, and public health consequences of this destructive disease. We at NIDA are proud to present this summary of our quarter century of progress, as we prepare to embark upon a new millennium of promise. ■



*NIDA moved to its new home at the Neuroscience Center in Bethesda, Maryland, in 1998.*

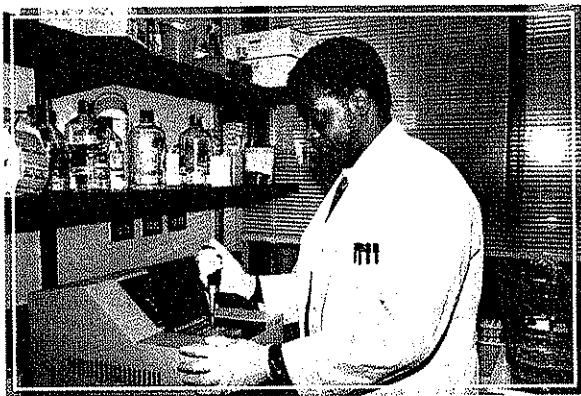
# A NIDA Chronology

## NIDA's Roots

NIDA traces its beginnings to a small research unit at a U.S. Public Health Service hospital in Lexington, Kentucky. The unit was created in 1935 to study and treat heroin addiction among Federal prisoners and others who voluntarily admitted themselves to the facility. That research unit, which conducted pioneering studies into the nature of the addictive process, essentially spawned the science of drug abuse research. The unit eventually became known as the Addiction Research Center and became NIDA's Intramural Research Program (IRP) when the Institute was created in 1974. NIDA's IRP now conducts research at its facilities in Baltimore.

## The 1970s

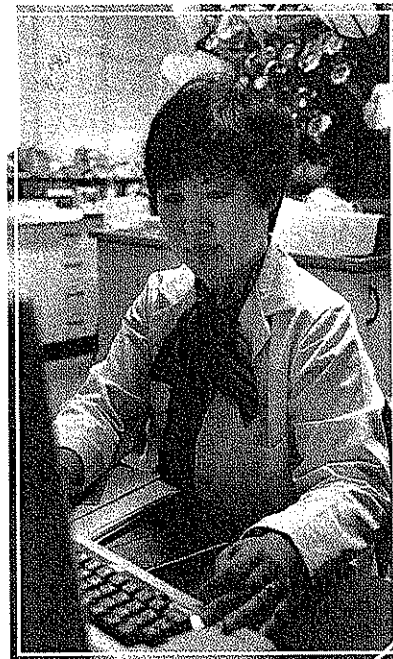
In 1974, NIDA was officially established by Congress as the Federal focal point for research to increase knowledge about drug abuse, promote effective strategies to deal with the problem, and develop and manage a nationwide network of drug abuse prevention, treatment, and training programs. NIDA initially focused much of its research on heroin addiction and its link to crime. However, the Institute soon inaugurated research, prevention, and treatment efforts aimed at the entire



Dr. Jean Lud Cadet of NIDA's Intramural Research Program has studied the effects of drugs on human memory.

range of drugs of abuse. Major events and accomplishments of the 1970s:

NIDA-supported scientists develop an animal model that shows that animals will self-administer most of the same drugs that people do. Researchers still use this model today to screen and characterize the abuse liability of new drugs and the treatment potential of new compounds being considered as drug abuse medications.



Dr. Nancy Lee's work at the University of California, San Francisco shed light on natural opioids in the brain.

NIDA scientists pioneer the development of urine drug testing methods. This research has led to methodologies that are widely used today to detect illicit drug use. They have provided drug abuse treatment researchers, physicians, and other health care providers with valuable diagnostic instruments and prevention tools.

NIDA-supported researchers make a series of groundbreaking discoveries about the brain and its molecular and neurochemical methods of communication. The discovery of opioid receptors in the body, identification of naturally occurring chemicals that act at these receptors to mediate mood and pain, and the finding that opiates such as heroin act at these same receptors revolutionized thinking about the addictive process and brain function in general.

The Institute initiates the Monitoring the Future Study. (See "Tracking Trends in Teen Drug Abuse Over the Years," p. 11)

NIDA establishes the first national-level surveillance network to assess current drug use patterns and identify emerging trends in major met-

ropolitan areas around the country. This network, called the Community Epidemiology Work Group (CEWG), has been meeting semiannually for more than 21 years. Using the CEWG model, a number of State Epidemiology Work Groups in the United States and an International Epidemiology Work Group now monitor drug use patterns and trends around the world.

**N**IDA undertakes comprehensive research on nicotine addiction to study how the drug is absorbed and distributed by the body. NIDA's nicotine research has defined the central role of nicotine in tobacco dependence and cigarette smoking, laid the groundwork for recent State and Federal actions to regulate the advertising and sale of tobacco products, and provided the scientific basis for the development of nicotine replacement therapies in the 1990s.



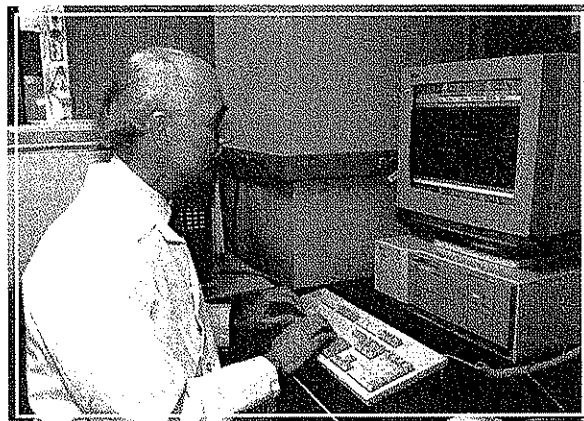
*Dr. Vis Navaratnam of the University of Science of Malaysia, at an international meeting of epidemiologic researchers, stresses that policymakers need accurate, timely information from drug abuse monitoring systems.*

**T**he Institute initiates research on the health and developmental consequences of prenatal drug exposure for infants and children. This research led to the development of a pharmacological treatment to ease newborn infants' withdrawal from prenatal exposure to narcotics. Today, NIDA

supports more than 30 long-term studies of the effects of women's use of narcotics, cocaine, and other drugs on pregnancy, maternal health, and infant and child development.

## The 1980s

**N**IDA's mission changed in 1981 when Congress legislated the Alcohol and Drug Abuse and Mental Health Services Block Grant Program, transferring to the States full responsibility for the delivery of drug abuse prevention and treatment



*Dr. Edward Cone examines hair analyses for cocaine as part of his research in NIDA's Intramural Research Program to improve drug testing methods.*

services. NIDA maintained primary responsibility for supporting and conducting research on drugs of abuse. Additional legislation charged NIDA with expanding its dissemination of research findings to States, localities, and community organizations around the country. Major events and accomplishments of the 1980s:

**A**IDS becomes a major NIDA research priority because of the central role that injection drug use plays in the transmission of HIV. From 1986 to 1987, NIDA's budget increased dramatically to support new research on both AIDS and drug abuse with AIDS funding nearly tripling. Among the effective responses developed by NIDA were the National AIDS Outreach Demonstration Projects. These projects provided out-of-treatment drug injectors and their sexual partners with AIDS prevention and education messages, encouraged drug users to enter drug abuse treatment, and demonstrated that drug users can reduce AIDS risk behaviors.

**A**n inexpensive, highly addictive, smokeable form of cocaine called "crack" makes its debut on the streets and spurs an epidemic of cocaine use. In response, NIDA expands basic and clinical research on cocaine and launches major cocaine prevention campaigns.

**E**xpanded basic research on cocaine pays off when NIDA's intramural researchers identify a

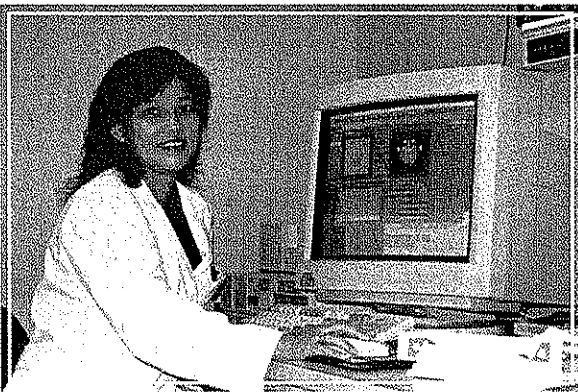
protein called the dopamine transporter as the primary site in the brain where cocaine acts to initiate the drug's euphoric and addictive effects. Today, NIDA-supported researchers are pursuing development of a number of promising cocaine treatment medications targeted at this brain molecule.

After years of NIDA-supported research in collaboration with the private sector, naltrexone joins methadone as the only medications approved by the Food and Drug Administration (FDA) for treating heroin addiction. Naltrexone blocks heroin's effects and is used to prevent relapse to drug use among recovering addicts.

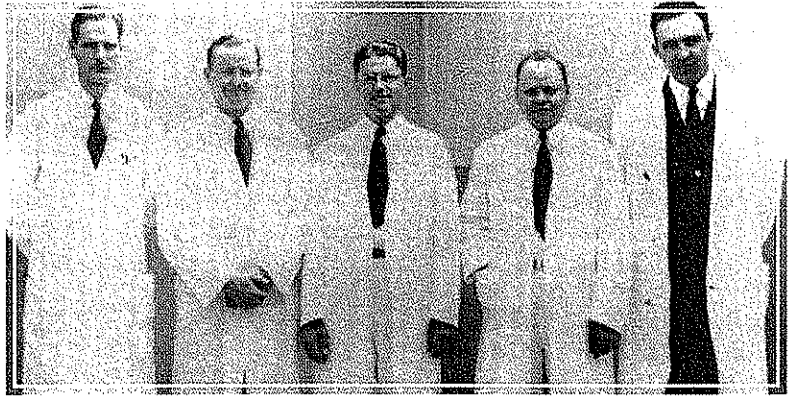
NIDA-supported researchers continue to build the scientific base for effective drug abuse prevention programs by identifying individual, family, school, and neighborhood factors that place children at risk for drug abuse and addiction. To date, researchers have identified a constellation of these risk factors and, equally important, a large number of protective factors that help to buffer the risk factors and reduce the likelihood that young people will abuse drugs. Drug abuse prevention researchers have since developed a broad array of effective family, school, and community programs that target these factors.

## The 1990s

In 1992, NIDA became part of the National Institutes of Health (NIH). This landmark event



Dr. Linda Chang of Harbor-UCLA Medical Center operates a computer program that combines brain images to study the interaction of cocaine and an HIV-induced brain infection.

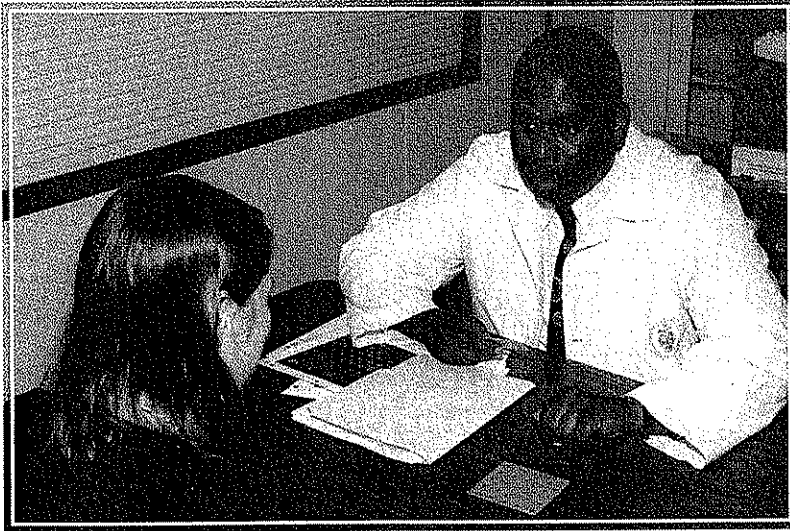


These pioneering drug abuse researchers worked at the Addiction Research Center (ARC), established in 1935 at a Public Health Service hospital in Lexington, Kentucky, and later to become NIDA's Intramural Research Program. From left, psychologist Ralph Brown, chemist Fred Oberst, psychologist and ARC's first director Clifton Himmelsbach, physiologist Edwin Williams, who would become ARC's second director, and biophysicist Howard Andrews.

affirmed both the quality of NIDA's research and its importance to the Nation's public health. As an NIH institute, NIDA has built on past research, engaged in collaborative research with other NIH institutes, and has seized the opportunities presented by new research technologies and methodologies in molecular biology, neuroscience, and brain imaging to accelerate the pace of scientific discoveries about drug abuse. Major events and accomplishments of the 1990s:

NIDA intramural and extramural researchers clone the dopamine transporter, cocaine's primary site of action in the brain. NIDA-supported researchers have since cloned the brain receptors at which every major drug of abuse acts to trigger the complex cascade of biochemical events that produces those drugs' psychoactive and behavioral effects. Researchers now use these cloned molecules to design and screen new compounds and medications approved for other conditions for possible efficacy as drug abuse treatments.

NIDA establishes its Medications Development Division (MDD). The Division's mission is to focus and expand efforts to develop new medications that can be combined with behavioral therapies to improve treatment of drug abuse and its consequences. In its short life span, MDD has seen



*Dr. Tony Strickland of Charles R. Drew University of Medicine and Science tests a volunteer for cocaine-related mental deficits.*

one opiate treatment medication through the FDA approval process (see LAAM, below) and filled NIDA's medications development pipeline with many other compounds that hold promise for treating cocaine, heroin, and methamphetamine abuse.

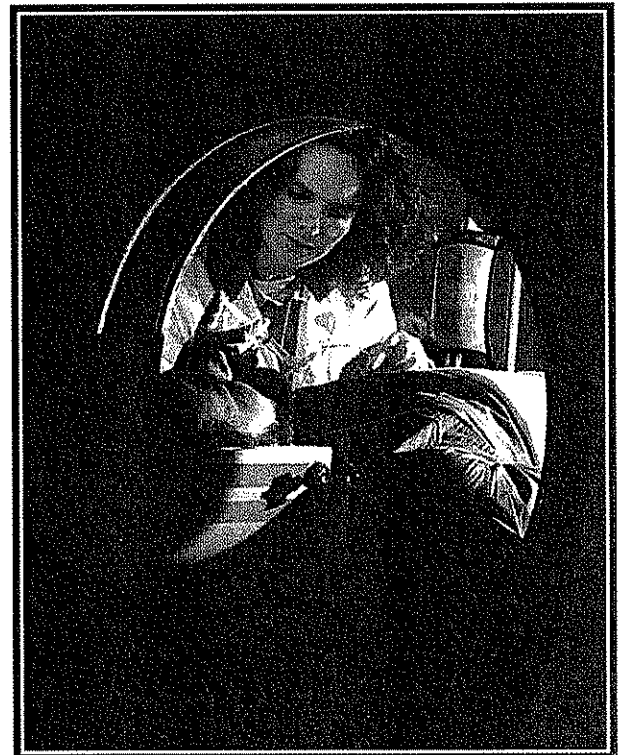
**M**DD successfully shepherds LAAM (levo-alpha-acetyl-methadol), a heroin treatment medication, through FDA's regulatory process. LAAM was the first new medication for the treatment of addiction to heroin and other opiates approved by FDA since the agency had approved naltrexone nearly a decade earlier. LAAM provides treatment practitioners with a long-acting alternative to methadone and is used to stabilize heroin addicts in long-term treatment. MDD currently has several heroin treatment medications, including buprenorphine and a longer acting form of naltrexone, in the latter stages of FDA approval.

**T**he Institute establishes its Behavioral Therapies Development Program. The program seeks to enhance existing behavioral treatments; develop, replicate, and standardize new behavioral therapies; and promote the use of those treatments that are effective in reducing drug abuse. The program has produced a host of science-based cognitive-behavioral treatments for

drug abuse and addiction, including new family therapies, relapse prevention approaches, brief motivational enhancement therapies, and improved counseling techniques.

**N**IDA inaugurates annual constituent conferences to obtain advice and recommendations on the Institute's activities from members of national organizations whose work is tied to drug abuse. Over the last 5 years, NIDA has implemented hundreds of activities, including major research initiatives, in direct response to constituents' concerns and recommendations about drug abuse issues.

**N**IDA expands research on women, gender, and drug abuse. Gender-based research now is integrated throughout NIDA's grant portfolio. The research seeks to identify the critical biological and behavioral factors that differentially affect the initiation, progression, and consequences of drug abuse and addiction in females and males of all



*Dr. Nora Volkow of NIDA's Regional Neuroimaging Center at Brookhaven National Laboratory prepares for a brain imaging session using positron emission tomography to examine how and where cocaine acts in the brain.*



*Dr. Christopher Evans, Duane Keith, and Dr. Robert H. Edwards, are members of the University of California, Los Angeles team that cloned the delta opioid receptor, one of the molecular sites in the brain where morphine binds.*

ages and how these variables should be addressed in drug abuse prevention and treatment.

A new brain imaging center opens at NIDA's IRP in Baltimore. This center, and NIDA's new Regional Neuroimaging Center at Brookhaven National Laboratory in Upton, New York, affirm NIDA's commitment to brain imaging as a vital drug abuse research tool. Brain imaging studies conducted by intramural and extramural researchers have greatly increased understanding of the neurobiological basis of drug abuse and addiction.

NIDA launches major marijuana, heroin, and methamphetamine research and communications initiatives to counter increases in the abuse of these drugs by younger and more diverse populations. These initiatives have buttressed NIDA's research to develop new targeted approaches to reducing the use of these three drugs and associated health problems. These initiatives also have increased dissemination of the latest scientific findings about these drugs and approaches that can be used to stem their use.

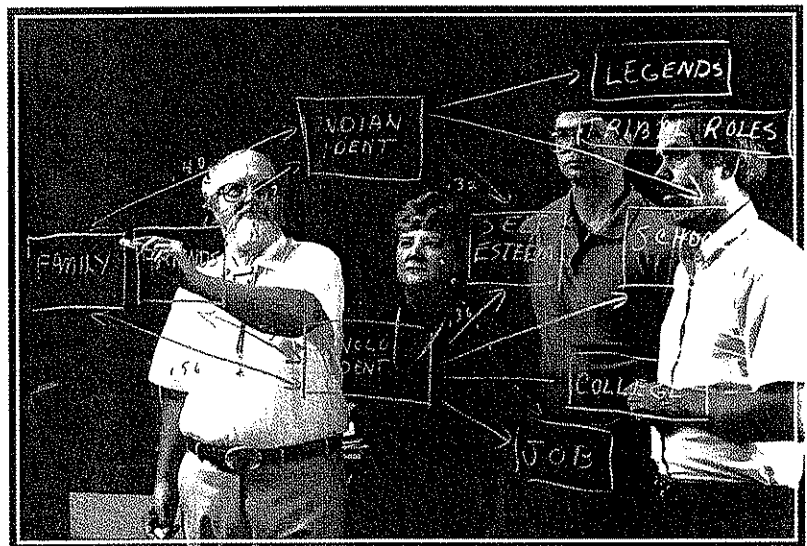
The National Conference on Drug Abuse Prevention Research is convened to spread the word about effective, science-based school, family, and community drug abuse prevention programs developed by NIDA-supported researchers. To further aid communities in apply-

ing research findings to their local drug abuse prevention efforts, NIDA published and disseminated the first research-based guide to preventing drug abuse among children and adolescents.

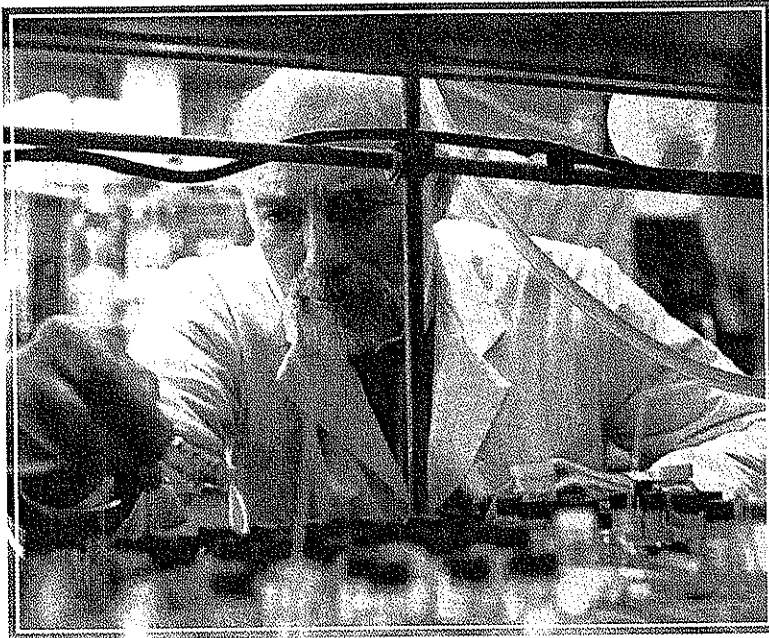
NIDA inaugurates a series of Town Meetings to bring the latest scientific findings about drug abuse to communities across the Nation. These meetings have been helping to bridge the "great disconnect," the gap between scientific knowledge about the nature of drug addiction as a chronic, relapsing brain disease and public perceptions that it is solely a behavioral or social problem.

NIDA's Drug Abuse Treatment Outcome Study (DATOS), a major nationwide study of drug abuse treatment outcomes in the 1990s, finds that the most common forms of drug abuse treatment programs all are effective in reducing drug use. DATOS data also show that treatment led to significant improvements in other aspects of patients' lives, such as increased full-time work and reduced involvement in illegal activities.

NIDA expands health services research to give drug abuse treatment and prevention service providers scientific data and research-based methodologies to gauge how well their programs



*Dr. Eugene Oetting and his colleagues at Colorado State University examine the role of cultural factors in drug abuse.*



*Dr. Philip Portoghese at the University of Minnesota conducts research on analgesics.*

work for patients in real-life settings. This research is giving service providers the tools to determine whether their programs provide cost-effective, accessible services that reduce drug abuse and addiction and related costs to society.

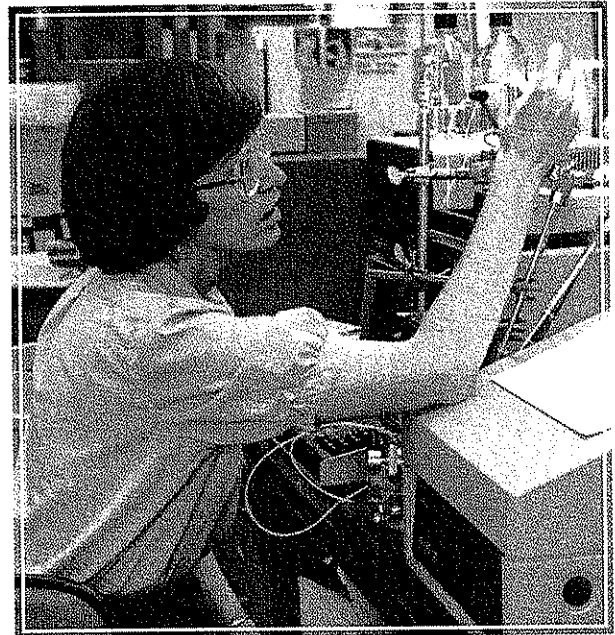
**T**o improve the quality of the Nation's drug abuse treatment, NIDA launches a Treatment Research

Initiative. The Initiative is synthesizing research-based knowledge about the treatment of drug abuse and addiction, expanding research to fill gaps in knowledge, and increasing dissemination of the latest treatment research findings.

**N**IDA establishes its Center on AIDS and Other Medical Consequences of Drug Abuse to address the full spec-

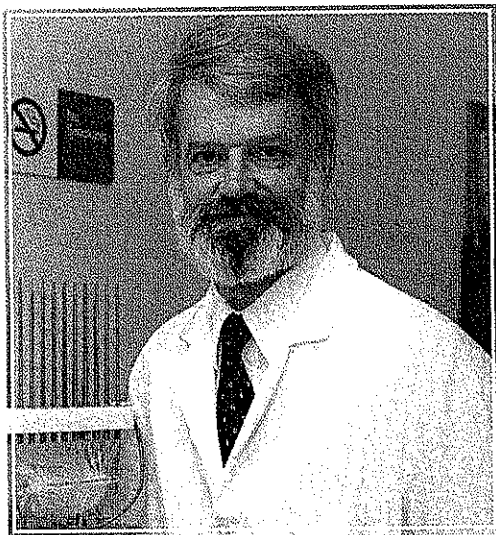
trum of health issues associated with drug abuse. The Center develops and coordinates multidisciplinary national and international research programs on the link between drug abuse and HIV/AIDS, hepatitis, tuberculosis, sexually transmitted diseases, mental health conditions, and other health problems.

**T**he Institute launches its Vulnerability to Addiction Initiative to increase knowledge of genetic and environmental factors and how they interact to increase or reduce vulnerability to drug abuse and addiction. Ultimately, the Initiative will increase understanding about the origins of drug abuse and addiction and provide knowledge that can be applied to the development of more effective drug abuse prevention and treatment strategies.



*Dr. Elizabeth Eipper's studies at The Johns Hopkins University increased understanding of the processes that produce brain peptides.*

**N**IDA begins to develop an extensive clinical trials network throughout the Nation to launch the next generation of drug abuse research. This network will establish a partnership between drug abuse treatment researchers and practitioners to test, refine, and speed the adoption of effective drug abuse treatments to enhance existing community-based treatment programs around the country. ■



*Dr. Billy Martin of Virginia Commonwealth University has explored the dependence potential of marijuana.*

## Tracking Trends in Teen Drug Abuse Over the Years

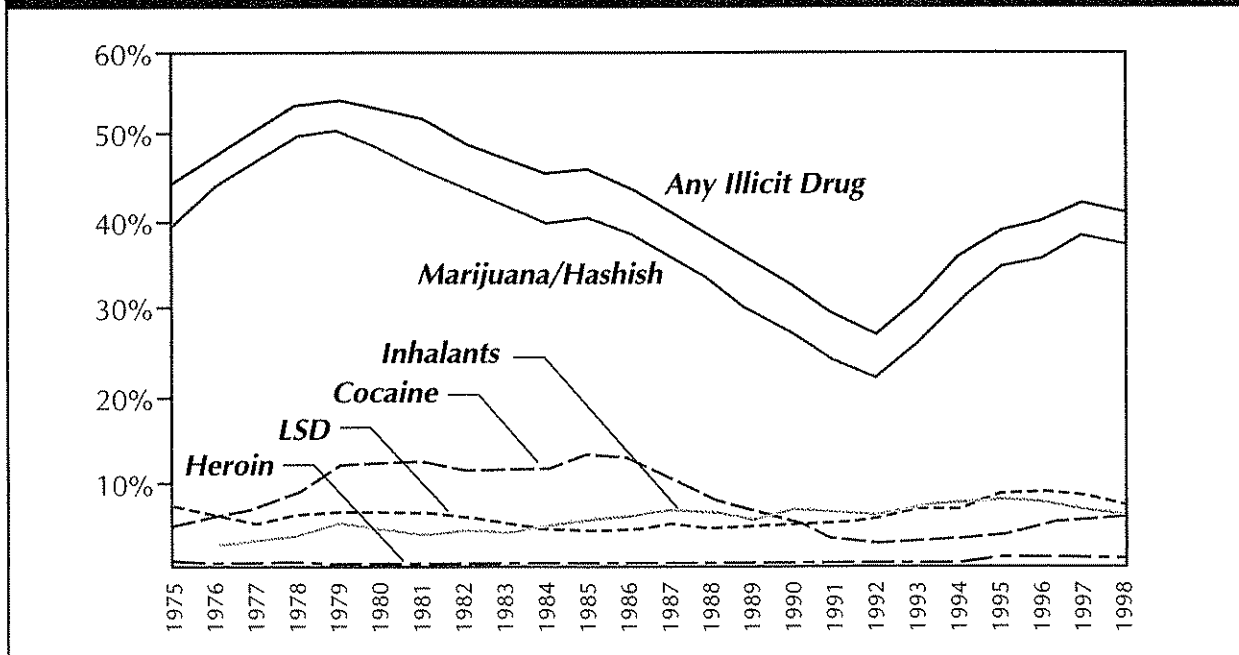
In 1975, shortly after NIDA was established, NIDA's first Monitoring the Future study (MTF) began to collect data on drug use among the Nation's high school seniors. In 1991, 8th- and 10th-grade students were added to the annual study to examine drug use among younger adolescents. Over the course of its 24-year history, MTF has charted some significant changes in illicit drug use among America's school-aged children. For example, some trends in annual use—use in the past year—include:

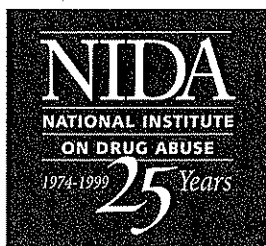
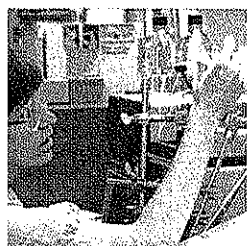
- Annual use of any illicit drug by high school seniors peaked at 54.2 percent in 1979, declined to a low of 27.1 percent in 1992, then climbed steadily to 42.4 percent in 1997. Seniors' use of any illicit drug has been stable since then.
- Annual marijuana use among high school seniors crested in 1979 at 50.8 percent, then declined to 21.9 percent in 1992, before rising steadily to 38.5 in 1997. Marijuana use by seniors has remained steady since then.

- Annual cocaine use more than doubled among high school seniors from 5.6 percent in 1975 to 13.1 percent in 1985 then declined sharply to 4.9 percent in 1996. Seniors' cocaine use has been stable since then.
- Heroin use always has been relatively low among school children. However, in recent years, the availability of cheap, high-purity heroin that enables users to get high by snorting the drug rather than injecting it has contributed to heroin use approximately doubling among high school seniors from 0.4 percent in 1991 to 1.0 percent in 1998.
- Marijuana, cocaine, and heroin use bottomed out in the early 1990s but has since risen among children at all grade levels. MTF figures for 1997 and 1998 suggest this trend toward increased illicit drug use is leveling off and may be in the process of reversing.

The Monitoring the Future study is funded by NIDA and conducted by the University of Michigan's Institute for Social Research.

### Trends in Past-year Use of Drugs by High School Seniors





*Where to Find*

## *Information About NIDA and Drug Abuse*

NIDA's Home Page on the Web: [www.nida.nih.gov](http://www.nida.nih.gov)

NIDA Infobox: **1-888-644-6432** (1-888-NIH-NIDA)

**TTY: 1-888-889-6432** (1-888-TTY-NIDA)

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