

## BI 358 Discussion Session 2

- :30 ***I. Group Discussion***: DLN 2-2 thru 2-6 *Eugene Weekly*  
112311 Fate of Medical Marijuana in OR? > WA + CO?
- :35 ***II. Class Convenes***: w/group summary statements.
- :40 ***III. Regroup*** (new groups!) for DLN review  
Try to incorporate general model of addiction after D.O.  
*Norris Simplified Homeostatic Model.*  
#1 Alcohol DLN 2-7 thru 2-12  
#2 Cocaine DLN 2-13 thru 2-20  
#3 Heroin DLN 2-21 thru 2-28  
#4 Marijuana DLN 2-29 thru 2-40  
#5 Methamphetamine DLN 2-41 thru 2-48  
#6 Tobacco/Nicotine DLN 2-49 thru 2-60
- :10 ***IV. Informal Group Overhead Presentations***



Paper Topic + 4 copies of Brief Outline due next T!  
Be sure to visit

<http://learn.genetics.utah.edu/content/addiction/drugs/mouse.html>

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# This bud's for who?

## Feds smoke the medical marijuana industry

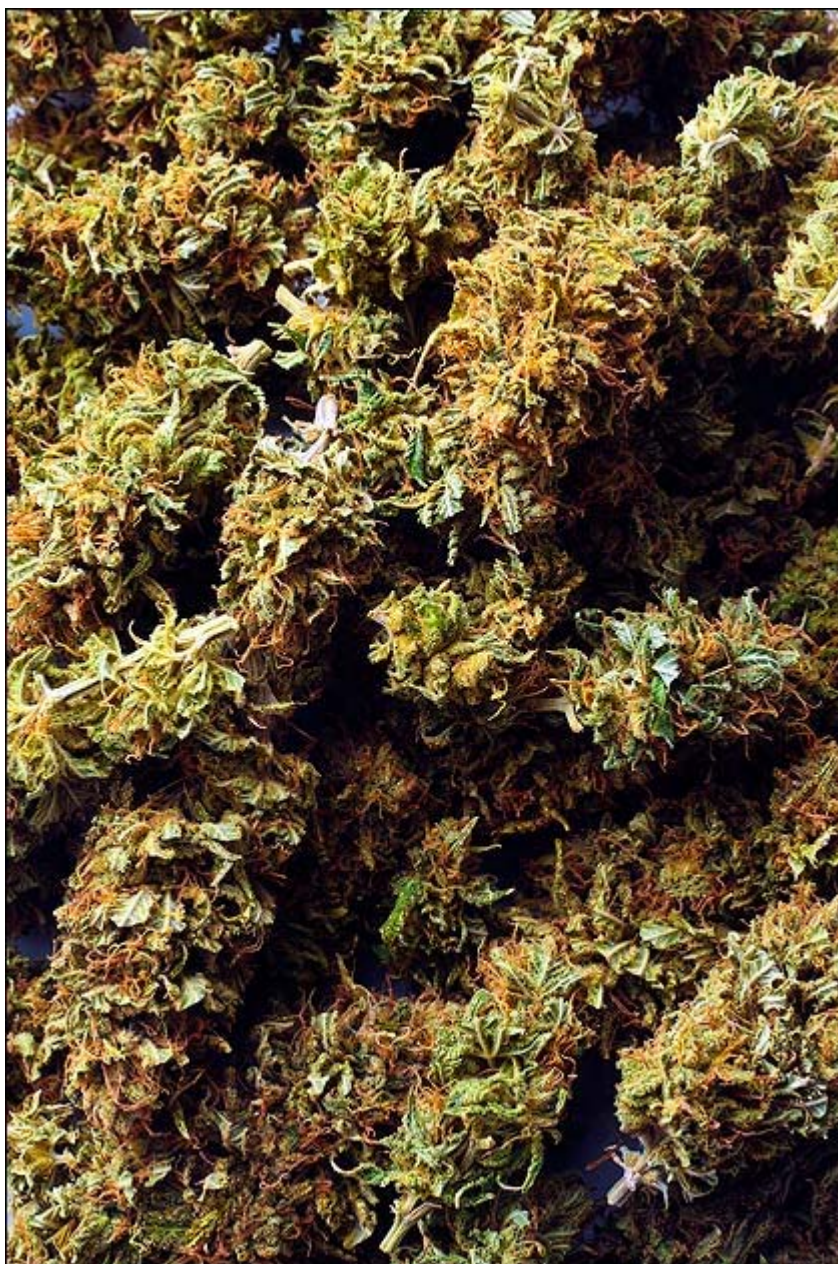
by Dante Zuñiga-West

**Medical marijuana users seeking to obtain their medicine in Oregon and throughout the country may soon find themselves asking the loaded question — Yo Obama, where's the weed at?**

Maybe you feel you have the right to experiment with your own consciousness. Perhaps you are one to promote the legalization of all illicit substances. Or it might be the case that you identify with the late R&B singer Nate Dogg, who once sang, "Hey ey ey ey, smoke weed everyday," based on the fact that you enjoy (as he did) the recreational use of cannabis.

That's your own damn business and has nothing to do with the medicinal purposes of the plant. This article is not the flag-waving counterculture anti-prohibitionist hotbox you are looking to occupy. Though compelling arguments exist on behalf of marijuana and Peter Tosh's iconic statement "Legalize it," the year 2011 has brought to bear a new series of issues for "legal" medicinal usage of the substance.

A concentrated effort to stamp out marijuana and the medical marijuana industry under the Obama administration has been sweeping the country this entire past year. Busts yielding significant and less than



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significant hauls of marijuana are happening up and down the coast at an intensified rate. But more precisely, the medical marijuana industry and its proponents are being targeted on a national scale.

The effect of this has made its way from Washington, D.C., all the way to the West Coast and to Eugene. Sept. 22, Oregon State Police arrested three men and seized 300 plants from two separate residences, in a raid that was part of an ongoing investigation by the Lane County Interagency Narcotics Enforcement Team.

## Up in the Club

It's estimated that legal marijuana is a \$10 billion to \$100 billion industry in the U.S. (the exact figure is unknown). Lane County is home to more than 5,000 card-carrying medical marijuana patients. Curtis Shimmin, owner of Kannabosm says he sees a demand for services such as that provided by Kannabosm.

“There is an incredible need for safe access to marijuana,” Shimmin says, “We are the only club here that does what we do.”

For a monthly membership fee of \$20, members of Kannabosm (all of whom must be card-carrying medical marijuana patients) receive access to their medication. The club also offers educational seminars on the medicinal properties of marijuana.

Kannabosm acts as a nexus connecting licensed growers and medical marijuana patients. Growers bring their harvest to the club and give permission to Kannabosm for patients to access it. A reimbursement fee is collected for the grower to cover the cost of production, though not labor.



Another service provided is a screening of the cannabis brought to the club, so as to ensure the herb is clean — meaning not laced with chemicals or polluted with pesticides.

“The counterculture image of marijuana doesn’t help this cause at all,” Shimmin says. “The goal is to provide safe access to medical marijuana, for medical marijuana patients. That’s the battle, and obviously I’m willing to take the risk.”

That risk is nothing short of federal prosecution.

“In the eyes of the law right now, what we are doing is illegal, but there is nothing that addresses whether or not we can do what we are doing,” Shimmin explains. “The law says you can use medical marijuana if you have a card, but then where do you get it?”

Shimmin says that without his club’s service, medical marijuana patients throughout Lane County would have no alternative but to buy weed on the black market or grow it themselves. “Ninety-nine percent of our clients are over the age of 60, and they’re not interested nor do they have the space or ability to grow for themselves,” he adds. “We have several stage-four cancer patients that practically crawl in here to get their meds.”

## Vaporizing the Industry

More so than clubs and dispensaries, it appears that wiping out marijuana grow operations has become a top priority to the Department of Justice this year. Detectives from the Spokane Sheriff’s office on Nov. 2 conducted a raid that turned up approximately 8 pounds of harvested marijuana, 695 marijuana plants and 500 additional recently harvested marijuana trimmings.

In Oregon’s northeastern Wallowa County, police and the Oregon Army National Guard seized and destroyed more than 91,000 marijuana plants in what is considered the biggest outdoor grow operation ever discovered in the state.

Also in Oregon, Nov. 18, near milepost 281, Oregon State Police stopped a California man headed northbound on Interstate 5 and seized 4 pounds of weed and 32 pounds of THC candy. Later that same day, a Salt Lake City man was pulled over and 2 pounds of marijuana were seized from his vehicle. Both drivers were arrested and jailed.

Alongside the big busts targeting growers, strategic blows to the infrastructure of medical marijuana are being meted out by the feds, particularly in California. One of the most high-profile of the aggressive nationwide measures enacted against the medical marijuana industry was the Oct. 7 announcement by four California U.S. attorneys declaring a crackdown that involved a multitude of enforcements against medical marijuana producers, distributors and the landlords leasing property to dispensaries.

If the aggressive crackdown carries over into Oregon, including threats such as the prosecution of newspapers and other media outlets that run advertisements for medical marijuana — things could get even sticky-ickier.

There is a saying that goes “what happens in California happens in Oregon a year later,” and if there is any truth to this colloquialism, it’s reasonable to assume Oregon is next in line on the fed’s medical marijuana hit list. Federal attention to Oregon’s medical marijuana issue actually came a bit earlier than Cali’s, though the assault has yet to be as focused.

Former U.S. district attorney for Oregon Dwight Holton sent a letter June 3 this year to all of Oregon's medical marijuana clubs urging them to "cease any distribution of marijuana in violation of federal law." The letter, which Kannabosm owner Curtis Shimmin received just four weeks after opening his doors, stated that the Department of Justice, along with district attorneys throughout Oregon, will "enforce federal law vigorously against individuals and organizations that participate in unlawful manufacture" or "distribution of marijuana."

Holton's warning, though it doesn't approach the severity of the measures being taken in California, is yet another sign of the Obama administration's nationwide blitz on the medical marijuana industry.

## Higher Forms of Health Care

Though the current national push to curtail or quash the medical marijuana industry made growers jumpy about speaking to a reporter, a look into the caretaker's role in the process allows for yet another side of the story to be heard.

Amber Younce, a nurse who works with advanced HIV patients at Our House of Portland, a center that provides health care, housing and other services for low-income people living with advanced HIV/AIDS, has encountered a significant number of medical marijuana patients.

Medical marijuana "has been incredibly important to AIDS patients trying to keep weight on and stay nourished," Younce says. "Other appetite stimulants don't work as well."

Younce also sees medical marijuana used to counteract negative side effects of other medications taken by her patients. Well aware of the disconnect between state and federal law concerning medical marijuana, Younce addresses the recent government push. "It's unfortunate there needs to be some new crackdown," she says. "It'd be great if the feds and the state could actually negotiate with each other, instead of putting law-abiding citizens at risk of criminal charges."

A negotiation of this sort would seem to be in the best interest of the feds, the states, law enforcement and the citizens, but the Obama administration has yet to address the issue head on. In fact, that the raids on growers and dispensaries have increased under Obama's presidency (particularly in California) appears to signal an opposite trend. If you are a medical marijuana patient, it sure looks like Obama is coming for your ganja. It's harvest season, but right now the only thing the DOJ wants you to smoke is your Thanksgiving turkey.

The Obama administration did seek to clarify the controversial "Odgen Memo," written in 2009 by Deputy U.S. Attorney General David Odgen, which originally stated that the federal government wouldn't mess with businesses operating in compliance with state laws regarding medical marijuana. And the new memo gives a nod to patients such as those Younce takes care of, stating that government resources will not be used to prosecute cancer patients or other terminally ill individuals who use marijuana in accordance with state law. Anyone else involved in the business of selling, growing or dispensing marijuana however, is operating in violation of the Controlled Substance Act.

Meaning, if you are a terminally ill medical marijuana patient, you can spark it up and burn one down, but good luck in the not-so-distant future grabbing your greenery from anywhere other than your friendly neighborhood dealer.

Is marijuana a hell of a drug? Apparently. Are people abusing both the substance as well as the ability to

get their hands on a card? Yes. But as Younce, who administers a smorgasbord of prescription drugs in her line of work, points out: “I’m not sure why we care that people are abusing it. People abuse every prescription drug there is.”

It remains unclear exactly why this push from the federal government is occurring now, at a time when Obama’s ratings aren’t so hot. Some activists speculate the aggressive measures against the medical marijuana industry are the result of pressure from law enforcement.

Though Oregon has yet to see the same level of smack down on medical marijuana as its neighbor to the south, there is no reason to believe that the state will avoid the same federal green-sweep increase within its borders. One thing is for certain: For now, weed and trouble still go together like bong and water.



U.S. Department of Health  
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National Institutes of Health

National Institute on Alcohol Abuse  
and Alcoholism

# ALCOHOL ALERT

Number 77

April 2009

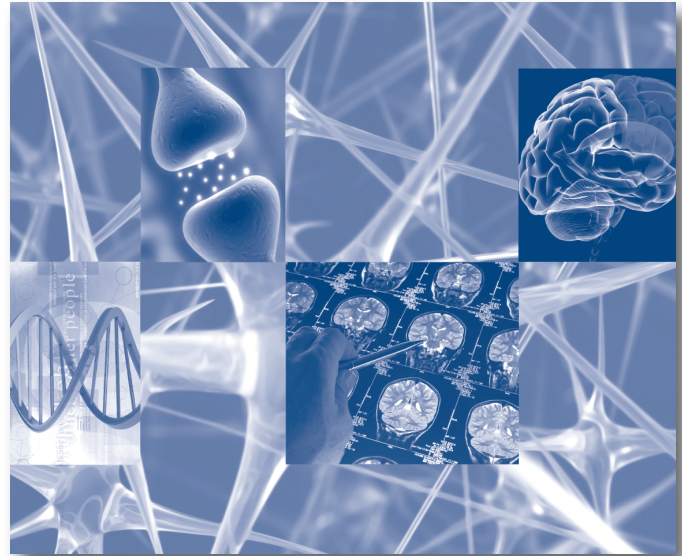
## NEUROSCIENCE: PATHWAYS TO ALCOHOL DEPENDENCE

Why does drinking alcohol have such profound effects on thought, mood, and behavior? And why does alcohol dependence develop and persist in some people and not in others? Scientists are addressing these questions and others through neuroscience—the study of the brain, where both alcohol intoxication and dependence begin. Through neuroscience research, scientists are gaining a better understanding of how alcohol changes the brain and how those changes in turn influence certain behaviors.

To function normally, the brain must maintain a careful balance of chemicals called neurotransmitters—small molecules involved in the brain's communication system that ultimately help regulate the body's function and behavior. Just as a heavy weight can tip a scale, alcohol intoxication can alter the delicate balance among different types of neurotransmitter chemicals and can lead to drowsiness, loss of coordination, and euphoria—hallmarks of alcohol intoxication.

Remarkably, with ongoing exposure to alcohol, the brain starts to adapt to these chemical changes. When alcohol is present in the brain for long periods—as with long-term heavy drinking—the brain seeks to compensate for its effects. To restore a balanced state, the function of certain neurotransmitters begins to change so that the brain can perform more normally in the presence of alcohol. These long-term chemical changes are believed to be responsible for the harmful effects of alcohol, such as alcohol dependence.

*“When alcohol is present in the brain for long periods—as with long-term heavy drinking—the brain seeks to compensate for its effects.”*



Today, thanks to rapidly advancing technology, researchers know more than ever about how alcohol affects the brain and how the brain responds and adapts to these effects. This *Alcohol Alert* summarizes some of what we know about alcohol's short- and long-term effects on the brain and how breakthroughs in neuroscience are leading to better treatments for alcohol-related problems.

### HOW ALCOHOL CHANGES THE BRAIN: TOLERANCE AND WITHDRAWAL

As the brain adapts to alcohol's presence over time, a heavy drinker may begin to respond to alcohol differently than someone who drinks only moderately. Some of these changes may be behind alcohol's effects, including alcohol tolerance (i.e., having to drink more in order to become intoxicated) (1) and alcohol withdrawal symptoms. These effects are associated with alcohol dependence.

When the brain is exposed to alcohol, it may become tolerant—or insensitive—to alcohol's effects. Thus, as a person

continues to drink heavily, he or she may need more alcohol than before to become intoxicated. As tolerance increases, drinking may escalate, putting a heavy drinker at risk for a number of health problems—including alcohol dependence.

Even as the brain becomes tolerant to alcohol, other changes in the brain may increase some people's sensitivity to alcohol. Desire for alcohol may transition into a pathological craving for these effects. This craving is strongly associated with alcohol dependence (1).

Other changes in the brain increase a heavy drinker's risk for experiencing alcohol withdrawal—a collection of symptoms that can appear when a person with alcohol dependence suddenly stops drinking. Withdrawal symptoms can be severe, especially during the 48 hours immediately follow-

ing a bout of drinking. Typical symptoms include profuse sweating, racing heart rate, and feelings of restlessness and anxiety (2). Research shows that alcohol-dependent people may continue drinking to avoid experiencing withdrawal. Feelings of anxiety associated with alcohol withdrawal can persist long after the initial withdrawal symptoms have ceased, and some researchers believe that—over the long term—this anxiety is a driving force behind alcohol-use relapse (3).

## THE BRAIN'S UNIQUE COMMUNICATION SYSTEM

Tolerance and withdrawal are tangible evidence of alcohol's influence on the brain. Scientists now understand some of the mechanisms that lead to these changes—changes that begin with the brain's unique communication system.

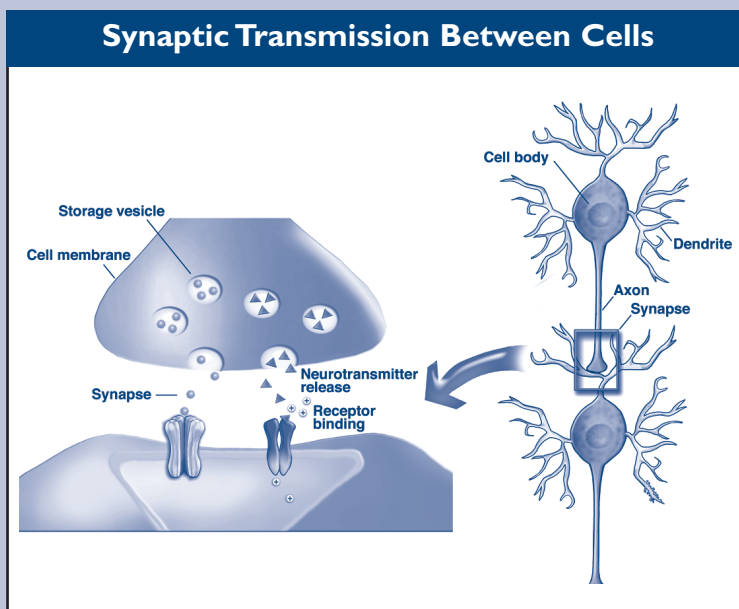
# NEURONS AND SYNAPTIC TRANSMISSION

The brain transmits information through a system of interconnected nerve cells known as neurons. Signals travel rapidly along chains of neurons using a combination of electrical and chemical processes. These signals cause many of alcohol's effects on behaviors, such as tolerance, craving, and addiction.

Signals travel from one neuron to the next through a process known as synaptic transmission. Synaptic transmission is made possible by the neuron's unique structure. In addition to a main cell body, neurons have two types of specialized thin branches: axons and dendrites. Axons transmit messages from one neuron to the next, and dendrites receive those messages from nearby neurons. Individual neurons are separated by tiny gaps known as synapses.

Messages travel from one neuron to the next across synaptic gaps and bind to special docking molecules on the receiving neuron's dendrites. These docking molecules are known as neurotransmitter receptors. When a neurotransmitter binds to a receptor, it changes the activity of the receiving neuron.

Depending on the situation, these changes might make the neuron either more likely or less likely to pass on, or "fire," the signal to the next neuron. If the signal is fired, it travels down the axon, sparking the release of more neurotransmitters into the next synapse and passing the signal along to the dendrites of the next neuron. If a signal is not fired, the signal stops.



SOURCE: Lovinger, D.M. Communication networks in the brain: Neurons, receptors, neurotransmitters, and alcohol. *Alcohol Research & Health* 31(3):196–214, 2008.



The brain communicates through a complex system of electrical and chemical signals. These signals are vital to brain function, sending messages throughout the brain, which, in turn, regulate every aspect of the body's function. Neurotransmitter chemicals play a key role in this signal transmission (4).

Under normal circumstances, the brain's balance of neurotransmitters allows the body and brain to function unimpaired. Alcohol can cause changes that upset this balance, impairing brain function. For example, the brain balances the activity of inhibitory neurotransmitters, which work to delay or stop nerve signals, with that of excitatory neurotransmitters, which work to speed up these signals. Alcohol can slow signal transmission in the brain, contributing to some of the effects associated with alcohol intoxication, including sleepiness and sedation.

As the brain grows used to alcohol, it compensates for alcohol's slowing effects by increasing the activity of excitatory neurotransmitters, speeding up signal transmission. In this way, the brain attempts to restore itself to a normal state in the presence of alcohol. If the influence of alcohol is suddenly removed (that is, if a long-term heavy drinker stops drinking suddenly), the brain may have to readjust once again: this may lead to the unpleasant feelings associated with alcohol withdrawal, such as experiencing "the shakes" or increased anxiety.

## NEUROTRANSMITTERS: A KEY TO EFFECTIVE MEDICATIONS FOR ALCOHOLISM

As researchers learn more about how neurotransmitters are involved in addiction, they can develop more effective medications that target specific neurotransmitter systems.

Unfortunately, there is no "magic bullet" for treating alcohol-related problems. It is unclear why some people respond well to certain medications, but others do not. However, exciting new research is helping scientists learn more about how alcohol affects different people. A handful of medications are now available to treat alcohol problems, many of which aim to alter

the short- or long-term effects of alcohol by either interfering with or imitating the actions of key neurotransmitters.

The table on page 4 provides information on some of the drugs used to treat alcohol withdrawal and dependence as well as brief descriptions of the neurotransmitter systems the drugs target. Scientists still are seeking to understand the details of how some of these medications work in the brain, but studies suggest that, in some people, they can be helpful in treating alcoholism and its consequences.

## NEW STRATEGIES FOR STUDYING ALCOHOL AND THE BRAIN

Powerful imaging methods now allow researchers to study how alcohol affects different brain systems and structures. Some of these methods include positron emission tomography (PET), event-related potentials (ERPs), and magnetic resonance imaging and magnetic resonance spectroscopy (MRI/MRS). These methods are especially useful because they allow researchers to see, in real time, how alcohol changes the human brain. These imaging techniques—when used with alcoholics, nonalcoholics, and children of alcoholics—may help identify genetic risk factors for alcoholism (5).

PET is being used to track the changes that alcohol use causes in specific neurotransmitter systems—changes that may be the cause of alcohol's short-term pleasurable effects (i.e., intoxication) and long-term detrimental effects (i.e., alcohol dependence) (6). PET technology allows researchers to see how these molecules behave. For example, researchers are using PET to track the activity of dopamine, a neurotransmitter believed to contribute to alcoholism. With this information, researchers can identify specific parts of the dopamine system that could be targeted for the development of medications to treat alcoholism (6).

Using ERP, researchers have identified markers that appear in the brains of alcoholics and in children of alcoholics (a population that is at high risk for developing alcoholism) (7; for a review, see 8). A marker is a distinct characteristic that can be associated with a certain group of people. Such markers may be useful for identifying people who are at risk

for alcoholism. For example, scientists have found that certain electrical currents in the brain (as measured by a brainwave called P300) are different in people who are at risk for alcoholism. Research shows that alcoholics have a blunted P300 brainwave; that is, the peak of the brainwave is much lower than in people without an alcohol use disorder. Moreover, this difference in P300 peak is evident in children of alcoholics even before they have taken their first drink. Certain markers linked to alcoholism also are

*“As researchers learn more about how neurotransmitters are involved in addiction, they can develop more effective medications that target specific neurotransmitter systems.”*

# MEDICATIONS FOR ALCOHOLISM

Food and Drug Administration Approved Medications	Treatment Use	Target Neurotransmitters	Effect
<b>Benzodiazepines</b> (Valium® and Xanax®)	Treating alcohol withdrawal	GABA ( $\gamma$ -aminobutyric acid)	Increases GABA activity, curbing the brain's "excitability" during its withdrawal from alcohol, allowing the brain to restore its natural balance.
<b>Disulfiram</b> (Antabuse®)	Preventing alcohol consumption	Main effect on alcohol metabolism rather than in the brain	Increases the concentration of acetaldehyde, a toxic byproduct that occurs when alcohol is broken down (i.e., metabolized) in the body. Excess amounts of this byproduct cause unpleasant symptoms, such as nausea and flushing of the skin.
<b>Naltrexone</b> (ReVia®, Vivitrol®, Naltrel®)	Reducing/ stopping drinking	Opioids	Blocks opioid receptors involved in the pleasant sensations associated with drinking.
<b>Acamprosate</b> (Campral®)	Enhancing abstinence	Glutamate	Thought to dampen glutamate activity and may reduce some of the hyper-excitability associated with alcohol withdrawal.

Promising Medications*	Original Use	Target Neurotransmitters	Potential Use
<b>Topiramate</b> (Topamax®)	Treating seizures	GABA and glutamate	Appears effective in reducing drinking in alcohol-dependent patients.
<b>Selective serotonin reuptake inhibitors (SSRIs)</b> (fluoxetine [Prozac®], sertraline [Zoloft®], and others)	Treating depression and anxiety	Serotonin	SSRIs have shown mixed results for treating alcoholics with depression. May reduce drinking in patients who developed alcohol dependence later in life.
<b>Ondansetron</b> (Zofran®)	Preventing nausea and vomiting	Serotonin	May reduce drinking in patients who developed alcohol dependence early in life.
<b>Baclofen</b> (Kemstro®, Lioresal®)	Treating muscle spasms	GABA	May have beneficial effects in encouraging abstinence, especially in alcoholic patients with liver cirrhosis.
<b>Quetiapine</b> (Seroquel®)	Sometimes used in treating psychiatric disorders	Dopamine and serotonin	Early-stage trials indicate quetiapine might be effective in increasing rates of abstinence, and to be especially useful in patients with severe alcoholism or in those who developed alcohol dependence early in life.

NOTE: \*Not yet approved for use in the treatment of alcohol use disorders.

SOURCES: Lovinger, D.M. Communication networks in the brain: Neurons, receptors, neurotransmitters, and alcohol. *Alcohol Research & Health* 31(3):196–214, 2008.  
 Krishnan-Sarin, S.; O'Malley, S.; and Krystal, J.H. Treatment implications: Using neuroscience to guide the development of new pharmacotherapies for alcoholism. *Alcohol Research & Health* 31(4):400–407, 2008.

## New Technology to Map Alcohol's Effects

**With magnetic resonance imaging (MRI)/magnetic resonance spectroscopy (MRS), researchers use a powerful magnetic field to generate a highly detailed “map” of the brain. For example, one technique, known as functional MRI (fMRI), allows researchers to “see” blood flow to specific regions in the brain and, thus, to identify which regions of the brain currently are active. Using this technique, researchers are exploring how alcohol affects brain function and how brain function changes as alcohol dependence develops over time (9).**

found with other mental health disorders, including drug use disorders, antisocial personality disorder, conduct disorder, and attention deficit hyperactivity disorder (for a review, see 8), suggesting that there may be a genetic connection among all of these disorders.

In addition to imaging studies, researchers also are using animals to study alcoholism. The results of these studies can help researchers better understand how to treat alcoholism in humans. In particular, animal models help scientists study the genetic links involved in alcoholism. Researchers can “turn off” genes that may be involved in alcohol addiction in laboratory animals, giving them insight into how these genes affect an animal’s behavior (10). For example, an animal model could show whether an animal will still seek alcohol once a specific gene has been turned off. Researchers also are able to work with small clusters of cells from animal brains and to study alcohol’s effects on a cellular level (11).

Animal studies allow researchers to explore how alcohol damages the brain and how the brain begins to recover from this damage with abstinence from drinking. Studies in rats show that heavy episodic drinking (i.e., “binge drinking”) can injure the brain by causing the death of neurons and other components (12). These brain injuries may cause some of the changes in thought and behavior that are associated with alcohol dependence in humans (13). Animal studies

suggest that the brain can recover at least partially from this damage. One method being investigated is the use of neural stem cells, which, over time, may help to rewire new neurons and repair damage to the brain’s communication system (14).

## CONCLUSION

Neuroscience is showing that the pathways of addiction are based in the brain. Using advanced techniques such as imaging methods and studies with animal models, researchers are learning more about how alcohol interacts with the brain’s communication system in different people. Innovative technology also is helping identify the changes that occur in the brain’s structure and function as a result of drinking, and how alcohol disrupts the brain’s delicate chemical balance. This information may help scientists understand why and how alcoholism develops in different populations and ultimately result in more effective and targeted therapies for alcohol abuse and dependence.

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## Resources

Source material for this *Alcohol Alert* originally appeared in *Alcohol Research & Health*, Volume 31, Number 3, 2008 and *Alcohol Research & Health*, Volume 31, Number 4, 2008.

- ▶ *Alcohol Research and Health 31(3): Neuroscience: Pathways to Alcohol Dependence Part I—Overview of the Neurobiology of Dependence.* The first issue in this special two-part series introduces what we know about alcohol's effects on the brain, and how these effects might lead to dependence. Articles explore the brain's complex communication systems, and how short- and long-term alcohol use can affect these systems. A special section highlights emerging technologies, such as brain imaging and animal studies, which are helping researchers to understand even more about alcohol's effects on the brain.
- ▶ *Alcohol Research and Health 31(4): Neuroscience: Pathways to Alcohol Dependence Part II—Neuroadaptation, Risk, and Recovery.* The second issue in this series describes how the brain's own adaptations to the presence of alcohol may play a key role in alcohol dependence, and how neuroscience is helping researchers target medications to help people at risk for alcohol use disorders. Other articles show how changes in the brain may lead to tolerance, withdrawal, and relapse to drinking.
- ▶ For these and other resources, visit NIAAA's Web site, [www.niaaa.nih.gov](http://www.niaaa.nih.gov)



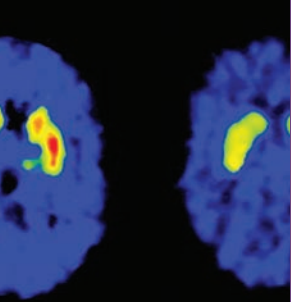
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Cocaine's stimulant and addictive effects explained. See page 2.

## Research Report Series

# Cocaine: Abuse and Addiction



## What Is Cocaine?

Cocaine is a powerfully addictive stimulant that directly affects the brain. Cocaine was labeled the drug of the 1980s and 1990s because of its extensive popularity and use during that period. However, cocaine is not a new drug. In fact, it is one of the oldest known psychoactive substances. Coca leaves, the source of cocaine, have been chewed and ingested for thousands of years, and the purified chemical, cocaine hydrochloride, has been an abused substance for more than 100 years. In the early 1900s, for example, purified cocaine was the main active ingredient in most of the tonics and elixirs

### from the director:

Cocaine abuse and addiction continue to plague our Nation. In 2008, almost 15 percent of Americans had tried cocaine, with 6 percent having tried it by their senior year of high school. Recent discoveries about the inner workings of the brain and the harmful effects of cocaine offer us unprecedented opportunities for addressing this persistent public health problem.

Genetic studies continue to provide critical information about hereditary influences on the risk of addiction to psychoactive substances, including cocaine. But genetic risk is far less rigid than previously thought. More recent epigenetic research has begun to shed light on the power of environmental factors (e.g., nutrition, chronic stress, parenting style) to influence gene expression and thus, genetic risk. Furthermore, sophisticated imaging technologies have allowed scientists to visualize the brain changes that result from chronic drug exposure or that occur when an addicted person is exposed to drug-associated "cues" that can trigger craving and lead to relapse. By mapping genetic factors, epigenetic mechanisms, and brain regions responsible for the multiple effects of cocaine, we are gaining fundamental insights that can help us identify new targets for treating cocaine addiction.

NIDA remains vigilant in its quest for more effective strategies to address the serious public health issues linked to cocaine abuse. We not only support a wide range of basic and clinical research, but also facilitate the translation of these research findings into real-world settings. To this end, we strive to keep the public informed of the latest scientific advances in the field of addiction. We hope that this compilation of scientific information on cocaine abuse will inform readers and bolster our efforts to tackle the personal and social devastation caused by drug abuse and addiction.

Nora D. Volkow, M.D.  
Director  
National Institute on Drug Abuse

that were developed to treat a wide variety of illnesses.

Pure cocaine was originally extracted from the leaf of the *Erythroxylon* coca bush, which grew primarily in Peru and Bolivia. After the 1990s, and following crop reduction efforts in those countries, Colombia became the nation with the largest cultivated coca crop. Today, cocaine is a Schedule II drug, which means that it has high potential for abuse but can be administered by a doctor for legitimate medical uses, such as local anesthesia for some eye, ear, and throat surgeries.

Cocaine is generally sold on the street as a fine, white, crystalline powder and is also known as “coke,” “C,” “snow,” “flake,” or “blow.” Street dealers generally dilute it with inert substances such as cornstarch, talcum powder, or sugar, or with active drugs such as procaine (a

chemically related local anesthetic) or amphetamine (another stimulant). Some users combine cocaine with heroin—in what is termed a “speedball.”

There are two chemical forms of cocaine that are abused: the water-soluble hydrochloride salt and the water-insoluble cocaine base (or freebase). When abused, the hydrochloride salt, or powdered form of cocaine, can be injected or snorted. The base form of cocaine has been processed with ammonia or sodium bicarbonate (baking soda) and water, and then heated to remove the hydrochloride to produce a smokable substance. The term “crack,” which is the street name given to freebase cocaine, refers to the crackling sound heard when the mixture is smoked.

Cocaine use ranges from occasional to repeated or compulsive use, with a variety of patterns between these extremes. Other than medical uses, there is no safe way to use cocaine. Any route of administration can lead to absorption of toxic amounts of cocaine, possible acute cardiovascular or cerebrovascular emergencies, and seizures—all of which can result in sudden death.

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## How Does Cocaine Produce Its Effects?

Research has led to a clear understanding of how cocaine produces its pleasurable effects and why it is so addictive. Scientists have discovered regions within the brain that are stimulated by all types of reinforcing stimuli such as food, sex, and many drugs of abuse. One neural system that appears to be most affected by cocaine originates in a region of the midbrain called the ventral tegmental area (VTA). Nerve fibers originating in the VTA extend to a region known as the nucleus accumbens, one of the brain’s key areas involved in reward. Animal studies show that rewards increase levels of the brain chemical (or neurotransmitter) dopamine, thereby increasing neural activity in the nucleus accumbens. In the normal communication process, dopamine is released by a neuron into the synapse (the small gap between two neurons), where it binds to specialized proteins (called dopamine receptors) on the neighboring neuron and sends a signal to that neuron. Dopamine is then

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## How Is Cocaine Abused?

The principal routes of cocaine administration are oral, intranasal, intravenous, and inhalation. Snorting, or intranasal administration, is the process of inhaling cocaine powder through the nostrils, where it is absorbed into the bloodstream through the nasal tissues. The drug also can be rubbed onto mucous tissues. Injecting, or intravenous use, releases the drug directly into the bloodstream and heightens the intensity of its effects. Smoking involves inhaling cocaine vapor or smoke into the lungs, where absorption into the bloodstream is as rapid as by injection. This rather immediate and euphoric effect is one of the reasons that crack became enormously popular in the mid-1980s.

Coca bush





removed from the synapse to be recycled for further use. Drugs of abuse can interfere with this normal communication process. For example, scientists have discovered that cocaine acts by blocking the removal of dopamine from the synapse, which results in an accumulation of dopamine and an amplified signal

to the receiving neurons (see image on page 4, “Cocaine in the brain”). This is what causes the initial euphoria commonly reported by cocaine abusers.

## What Are the Short-Term Effects of Cocaine Use?

Cocaine’s effects appear almost immediately after a single dose and disappear within a few minutes to an hour. Taken in

small amounts, cocaine usually makes the user feel euphoric, energetic, talkative, and mentally alert, especially to the sensations of sight, sound, and touch. It can also temporarily decrease the need for food and sleep. Some users find that the drug helps them perform simple physical and intellectual tasks more quickly, although others experience the opposite effect.

The duration of cocaine’s euphoric effects depend upon the route of administration. The faster the drug is absorbed, the more intense the resulting high, but also

## What Is the Scope of Cocaine Use in the United States?

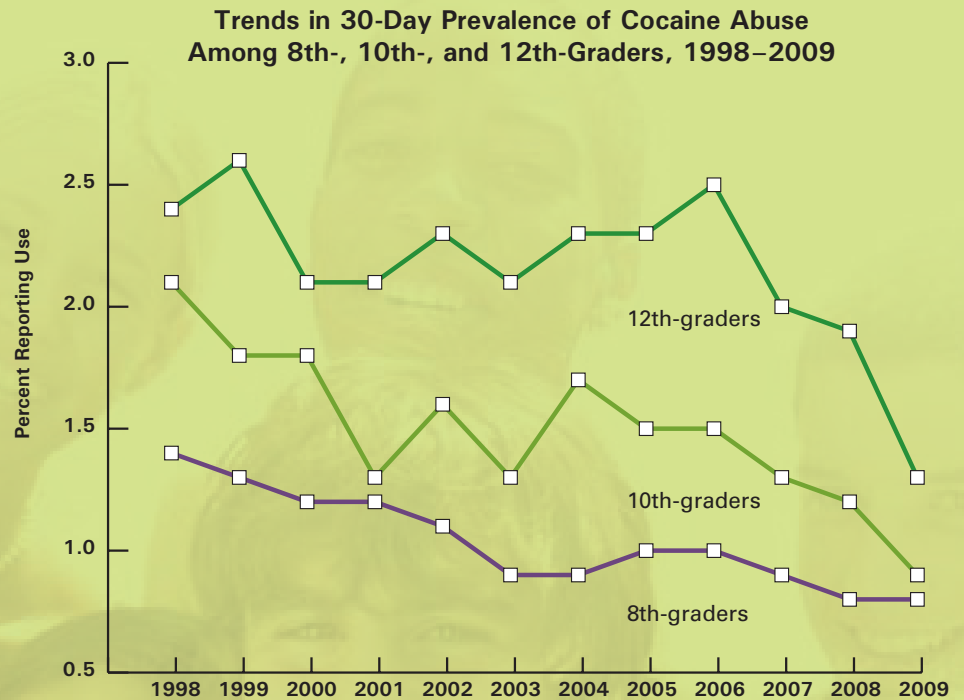
The National Survey on Drug Use and Health (NSDUH) estimates that in 2008 there were 1.9 million current (past month) cocaine users, of which approximately 359,000 were current crack users. Adults aged 18 to 25 years have a higher rate of current cocaine use than any other age group, with 1.5 percent of young adults reporting past-month cocaine use. Overall, men report higher rates of current cocaine use than women.

The 2009 Monitoring the Future survey, which annually surveys teen attitudes and drug use, reports a significant decline in 30-day prevalence of powder cocaine use among 8th-, 10th-, and 12th-graders from peak use in the late 1990s, as well as significant declines in past-month use among 10th- and 12th-graders from 2008 to 2009.

Repeated cocaine use can produce addiction and other adverse health consequences. In 2008, according

to the NSDUH, about 1.4 million Americans met the *Diagnostic and Statistical Manual of Mental Disorders* criteria for dependence or abuse of cocaine (in any form) in the past 12 months. Further, data from the 2008 Drug Abuse Warning Network (DAWN) report showed that cocaine was involved

in 482,188 of the nearly 2 million visits to emergency departments for drug misuse or abuse. This translates to almost one in four drug misuse or abuse emergency department visits (24 percent) that involved cocaine.



Source: University of Michigan, 2009 Monitoring the Future Survey.

the shorter the duration. The high from snorting is relatively slow to arrive, but it may last from 15 to 30 minutes; in contrast, the effects from smoking are more immediate but may last only 5 to 10 minutes.

The short-term physiological effects of cocaine use include constricted blood vessels; dilated pupils; and increased body temperature, heart rate, and blood pressure. Large amounts of cocaine may intensify the user's high but can also lead to bizarre, erratic, and violent behavior. Some cocaine users report feelings of restlessness, irritability, anxiety, panic, and paranoia. Users may also experience tremors, vertigo, and muscle twitches.

There also can be severe medical complications associated with cocaine abuse. Some of the most frequent are cardiovascular effects, including disturbances in heart rhythm and heart attacks; neurological effects, including strokes, seizures, headaches, and coma; and gastrointestinal complications, including abdominal pain and nausea. In rare instances, sudden death can occur on the first use of cocaine or unexpectedly thereafter. Cocaine-related deaths are often a result of cardiac arrest or seizures followed by respiratory arrest.

In addition, research has also revealed a potentially dangerous interaction between cocaine and alcohol. This mixture is the most common two-drug combination that results in drug-related death.

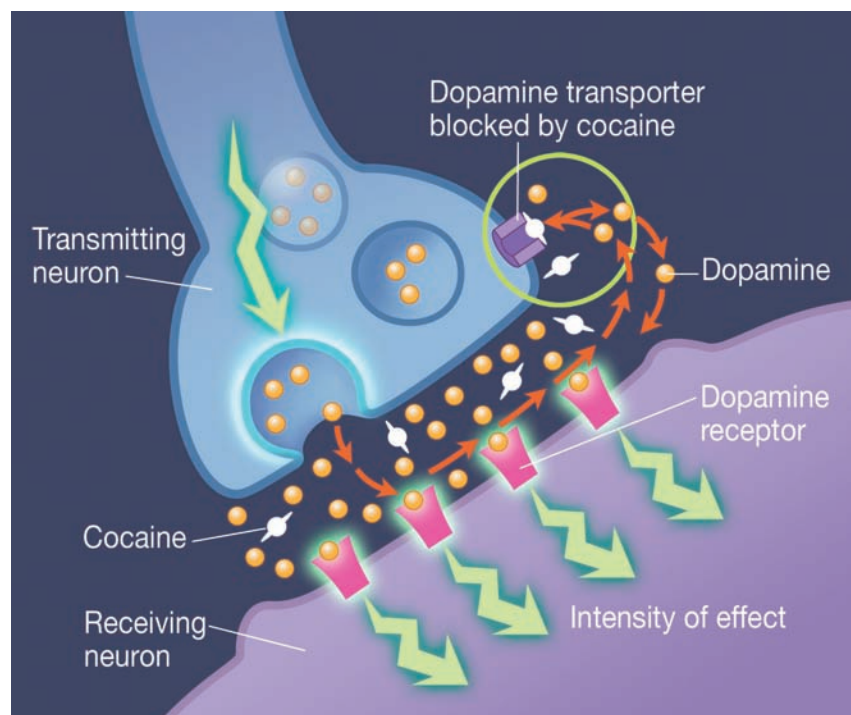
## What Are the Long-Term Effects of Cocaine Use?

Cocaine is a powerfully addictive drug. Thus, it is unlikely that an individual will be able to reliably predict or control the extent to which he or she will continue to want or use the drug. And, if addiction takes hold, the risk for relapse is high even following long periods of abstinence. Recent studies have shown that during periods of abstinence, the memory of the cocaine experience or exposure to cues associated with drug use can trigger tremendous craving and relapse to drug use.

With repeated exposure to cocaine, the brain starts to adapt, and the reward pathway becomes less sensitive to natural reinforcers and to the drug itself. Tolerance may develop—this means that higher doses and/or more frequent use of cocaine is needed to register the same level of pleasure experienced during initial use. At the same time, users can also become more sensitive (sensitization) to cocaine's anxiety-producing, convulsant, and other toxic effects.

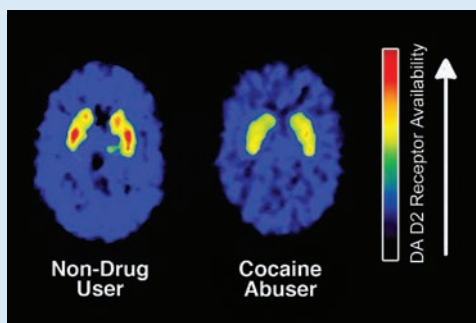
Users take cocaine in "binges," during which the cocaine is used repeatedly and at increasingly higher doses. This can lead to increased irritability, restlessness, panic attacks, and paranoia—even a full-blown psychosis, in which the individual loses touch with reality and experiences auditory hallucinations. With increasing dosages or frequency of use, the risk of adverse psychological or physiological effects increases.

Different routes of cocaine administration can produce different adverse effects. Regularly snorting cocaine, for example, can lead to loss of sense of smell; nosebleeds; problems with swallowing;



**Cocaine in the brain**—In the normal communication process, dopamine is released by a neuron into the synapse, where it can bind to dopamine receptors on neighboring neurons. Normally, dopamine is then recycled back into the transmitting neuron by a specialized protein called the dopamine transporter. If cocaine is present, it attaches to the dopamine transporter and blocks the normal recycling process, resulting in a buildup of dopamine in the synapse, which contributes to the pleasurable effects of cocaine.





Brain images showing decreased dopamine (D<sub>2</sub>) receptors in the brain of a person addicted to cocaine versus a nondrug user. The dopamine system is important for conditioning and motivation, and alterations such as this are likely responsible, in part, for the diminished sensitivity to natural rewards that develops with addiction.

hoarseness; and an overall irritation of the nasal septum, which could result in a chronically inflamed, runny nose. Ingested cocaine can cause severe bowel gangrene due to reduced blood flow. Persons who inject cocaine have puncture marks called “tracks,” most commonly in their forearms, and may experience allergic reactions, either to the drug or to some additive in street cocaine, which in severe cases can result in death. Many chronic cocaine users lose their appetite and experience significant weight loss and malnourishment.

## Are Cocaine Abusers at Risk for Contracting HIV/AIDS and Hepatitis?

Yes, cocaine abusers are at increased risk for contracting such infectious diseases as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and viral hepatitis. This risk stems not only from sharing contaminated needles and drug paraphernalia but also from engaging in risky behaviors as a result of intoxication. Research has shown that drug intoxication and addiction can compromise judgment and decisionmaking,

and potentially lead to risky sexual encounters, needle sharing, and trading sex for drugs—by both men and women. In fact, some studies are showing that among drug abusers, those who do not inject drugs are contracting HIV at rates equal to those who do inject drugs, further highlighting the role of sexual transmission of HIV in this population.

Additionally, hepatitis C (HCV) has spread rapidly among injecting drug users. Risk begins with the first injection, and within 2 years, nearly 40 percent of injection drug users (IDUs) are exposed to HCV. By the time IDUs have been injecting for 5 years, their chances of being infected with HCV are between 50 and 80 percent. Although treatment for HCV is not effective for everyone and can have significant side effects, medical followup is essential for all those who are infected. There is no vaccine for the hepatitis C virus, and it is highly transmissible via injection; thus, HCV testing is recommended for any individual who has ever injected drugs.

## What Treatments Are Effective for Cocaine Abusers?

In 2007, cocaine accounted for about 13 percent of all admissions to drug abuse treatment programs.

The majority of individuals (72 percent in 2007) who seek treatment for cocaine abuse smoke crack and are likely to be polydrug abusers, or users of more than one substance. The widespread abuse of cocaine has stimulated extensive efforts to develop treatment programs for cocaine. As with any drug addiction, this is a complex disease that involves biological changes in the brain as well as myriad social, familial, and other environmental problems. Therefore, treatment of cocaine addiction must be comprehensive, and strategies need to assess the neurobiological, social, and medical aspects of the patient’s drug abuse. Moreover, patients who have a variety of addictions often have other co-occurring mental disorders that require additional behavioral or pharmacological interventions.

### Pharmacological Approaches

Presently, there are no FDA-approved medications to treat cocaine addiction. Consequently, NIDA is working aggressively to identify and test new medications to treat cocaine addiction safely and effectively. Several medications marketed for other diseases (e.g., vigabatrin, modafinil, tiagabine, disulfiram, and topiramate) show promise and have been reported to reduce cocaine use in controlled clinical trials. Among these, disulfiram (used to treat alcoholism) has produced the most consistent reductions in cocaine abuse. On the other hand, new knowledge of how the brain is changed by cocaine is directing attention to novel targets for medications development. Compounds that are currently being tested for addiction treatment take advantage of underlying cocaine-induced adaptations in the brain that disturb the balance between excitatory (glutamate) and inhibitory (gamma-aminobutyric acid) neurotransmission. Also,

## What Are the Effects of Maternal Cocaine Use?

The full extent of the effects of prenatal cocaine exposure on a child is not completely known, but many scientific studies have documented that babies born to mothers who abuse cocaine during pregnancy are often prematurely delivered, have low birth weights and smaller head circumferences, and are shorter in length than babies born to mothers who do not abuse cocaine.

Nevertheless, it is difficult to estimate the full extent of the consequences of maternal drug abuse and to determine the specific hazard of a particular drug to the unborn child. This is because multiple factors—



such as the amount and number of *all* drugs abused, including nicotine; extent of prenatal care; possible neglect or abuse of the child; exposure to violence in the environment; socioeconomic conditions; maternal nutrition; other health conditions; and exposure to sexually transmitted diseases—can all interact to impact maternal, fetal, and child outcomes.

Some may recall that “crack babies,” or babies born to mothers who abused crack cocaine while pregnant, were at one time written off as a lost generation. They were predicted to suffer from severe, irreversible damage, including reduced intelligence and social skills. It was later found that this was a gross exaggeration. However, the fact that most of these children appear normal should not be overinterpreted to indicate that there is no cause for concern. Using sophisticated technologies, scientists are now finding that exposure to cocaine during fetal development may lead to subtle, yet significant, later deficits in some children, including deficits in some aspects of cognitive performance, information processing, and attention to tasks—abilities that are important for the realization of a child’s full potential.

dopamine D<sub>3</sub> receptors (a subtype of dopamine receptor) constitute a novel molecular target of high interest. Medications that act at these receptors are now being tested for safety in humans. Finally, a cocaine vaccine that prevents entry of cocaine into the brain holds great promise for reducing the risk of relapse. In addition to treatments for addiction, medical treatments are being developed to address the acute emergencies that result from cocaine overdose each year.

### Behavioral Interventions

Many behavioral treatments for cocaine addiction have proven to be effective in both residential and outpatient settings. Indeed, behavioral therapies are often the only available and effective treatments for many drug problems, including stimulant addictions. However, the integration of behavioral and pharmacological treatments may ultimately prove to be the most effective approach.

***Presently, there are no proven medications to treat cocaine addiction. Consequently, NIDA is working aggressively to identify and test new medications.***

One form of behavioral therapy that is showing positive results in cocaine-addicted populations is contingency management, or motivational incentives (MI). MI may be particularly useful for helping patients achieve initial abstinence from cocaine and for helping patients stay in treatment. Programs use a voucher or prize-based system that rewards patients who abstain from cocaine and other drug use. On the basis of drug-free urine tests, the patients earn points, or chips, which can be exchanged for items that encourage healthy living, such as a gym membership, movie tickets, or dinner at a local

restaurant. This approach has recently been shown to be practical and effective in community treatment programs.

Cognitive-behavioral therapy (CBT) is an effective approach for preventing relapse. CBT is focused on helping cocaine-addicted individuals abstain—and remain abstinent—from cocaine and other substances. The underlying assumption is that learning processes play an important role in the development and continuation of cocaine abuse and addiction. These same learning processes can be harnessed to help individuals reduce drug use and successfully prevent relapse. This approach attempts to help patients recognize, avoid, and cope; that is, they recognize the situations in which they are most likely to use cocaine, avoid these situations when appropriate, and cope more effectively with a range of problems and problematic behaviors associated with drug abuse. This therapy is also noteworthy because of its compatibility with a range

of other treatments patients may receive.

Therapeutic communities (TCs), or residential programs, offer another alternative to persons in need of treatment for cocaine addiction. TCs usually require a 6- or 12-month stay and use the program's entire "community" as active components of treatment. They can include onsite vocational rehabilitation and other supportive

services and focus on successful re-integration of the individual into society.

Community-based recovery groups—such as Cocaine Anonymous—that use a 12-step program can also be helpful to people trying to sustain abstinence. Participants may benefit from the supportive fellowship and from sharing with those experiencing common problems and issues.

It is important that patients receive services that match all of their treatment needs. For example, if a patient is unemployed, it may be helpful to provide vocational rehabilitation or career counseling along with addiction treatment. If a patient has marital problems, it may be important to offer couples counseling.

## Glossary

**Addiction:** A chronic, relapsing disease characterized by compulsive drug seeking and use and by long-lasting changes in the brain.

**Anesthetic:** An agent that causes insensitivity to pain and is used for surgeries and other medical procedures.

**Coca:** The plant, *Erythroxylon*, from which cocaine is derived. Also refers to the leaves of this plant.

**Crack:** The slang term for a smokable form of cocaine.

**Craving:** A powerful, often uncontrollable, desire for drugs.

**Dopamine:** A brain chemical, classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

**Freebase:** A solid, water-insoluble, and smokable form of cocaine that is produced when its hydrochloride salt form is processed with ammonia or sodium bicarbonate and water, then heated to remove the hydrochloride. (Also, see "crack.")

**Frontal cortex:** The front part of the brain involved with reasoning, planning, problemsolving, and other higher cognitive functions.

**Gamma-aminobutyric acid (GABA):** The main inhibitory neurotransmitter in the central nervous system. GABA provides the needed counterbalance to the actions of other systems, particularly the excitatory neurotransmitter glutamate.

**Glutamate:** An excitatory neurotransmitter found throughout the brain that influences the reward system and is involved in learning and memory, among other functions.

**Hydrochloride salt:** A powdered, water-soluble form of cocaine that can be injected or snorted.

**Neuron:** A nerve cell.

**Nucleus accumbens:** A brain region involved in motivation and reward. Nearly all drugs of abuse directly or indirectly increase dopamine in the nucleus accumbens, contributing to their addictive properties.

**Polydrug user:** An individual who uses more than one drug.

**Rush:** A surge of pleasure (euphoria) that rapidly follows the administration of some drugs.

**Stimulant:** A class of drugs that enhances the activity of monoamines (such as dopamine) in the brain, increasing arousal, heart rate, blood pressure, and respiration, and decreasing appetite; includes some medications used to treat attention-deficit hyperactivity disorder (e.g., methylphenidate and amphetamines), as well as cocaine and methamphetamine.

**Tolerance:** A condition in which higher doses of a drug are required to produce the same effect achieved during initial use.

**Vertigo:** The sensation of dizziness.

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## Where Can I Get More Scientific Information About Cocaine Abuse and Addiction?

To learn more about cocaine and other drugs of abuse, or to order materials on these topics free of charge in English or Spanish, visit the NIDA Web site at [www.drugabuse.gov](http://www.drugabuse.gov) or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).



### What's New on the NIDA Web Site

- Information on drugs of abuse
- Publications and communications (including *NIDA Notes* and *Addiction Science & Clinical Practice* journal)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

### NIDA Web Sites

[drugabuse.gov](http://drugabuse.gov)  
[backtoschool.drugabuse.gov](http://backtoschool.drugabuse.gov)  
[teens.drugabuse.gov](http://teens.drugabuse.gov)

### For Physician Information

**NIDAMED**   
[www.drugabuse.gov/nidamed](http://www.drugabuse.gov/nidamed)

### Other Web Sites

Information on cocaine abuse and addiction is also available through the following Web site:

- Substance Abuse and Mental Health Services Administration Health Information Network: [www.samhsa.gov/shin](http://www.samhsa.gov/shin)

## U.S. Department of Health and Human Services

NATIONAL INSTITUTES OF HEALTH

**NIDA** NATIONAL INSTITUTE  
ON DRUG ABUSE

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Feel free to reprint this publication.

# Research Report

SERIES

*Heroin is a highly addictive drug, and its abuse has repercussions that extend far beyond the individual user. The medical and social consequences of drug abuse—HIV/AIDS, tuberculosis, fetal effects, crime, violence, and disruptions in family, workplace, and educational environments—have a devastating impact on society and cost billions of dollars each year.*

*Although heroin abuse has trended downward during the past several years, its prevalence is still higher than in the early 1990s. These relatively high rates of abuse, especially among school-age youth, and the glamorization of heroin in music and films make it imperative that the public has the latest scientific information on this topic. Heroin also is increasing in purity and decreasing in price, which makes it an attractive option for young people.*

*Like many other chronic diseases, addiction can be treated. Fortunately, the availability of treatments to manage opiate addiction and the promise from research of new and effective behavioral and pharmacological therapies provides hope for individuals who suffer from addiction and for those around them. For example, buprenorphine, approved by the Food and Drug Administration (FDA) in 2002, provides a less addictive alternative to methadone maintenance, reduces cravings with only mild withdrawal symptoms, and can be prescribed in the privacy of a doctor's office.*

*The National Institute on Drug Abuse (NIDA) has developed this publication to provide an overview of the state of heroin abuse and addiction. We hope this compilation of scientific information on heroin will help to inform readers about the harmful effects of heroin abuse and addiction as well as assist in prevention and treatment efforts.*

Nora D. Volkow, M.D.  
 Director  
 National Institute on Drug Abuse

from the director

## HEROIN Abuse and Addiction

### What is heroin?

**H**eroin is an illegal, highly addictive drug. It is both the most abused and the most rapidly acting of the opiates. Heroin is processed from morphine, a naturally occurring substance extracted from the seed pod of certain varieties of poppy plants. It is typically sold as a white or brownish powder or as the black sticky substance known on the streets as “black tar heroin.” Although purer heroin is becoming more common, most street heroin is “cut” with other drugs or with substances such as sugar, starch, powdered milk, or quinine. Street heroin can also be cut with strychnine

or other poisons. Because heroin abusers do not know the actual strength of the drug or its true contents, they are at risk of overdose or death. Heroin also poses special problems because of the transmission of HIV and other diseases that can occur from sharing needles or other injection equipment.

### What is the scope of heroin use in the United States?

**A**ccording to the 2003 National Survey on Drug Use and Health, which may actually underestimate illicit opiate (heroin) use, an estimated 3.7 million people had used heroin at some time in their lives, and over 119,000 of them reported using it within the month preceding the survey. An estimated 314,000 Americans used



heroin in the past year, and the group that represented the highest number of those users were 26 or older. The survey reported that, from 1995 through 2002, the annual number of new heroin users ranged from 121,000 to 164,000. During this period, most new users were age 18 or older (on average, 75 percent) and most were male. In 2003, 57.4 percent of past year heroin users were classified with dependence on or abuse of heroin, and an estimated 281,000 persons received treatment for heroin abuse.

According to the Monitoring the Future survey, NIDA's nationwide annual survey of drug use among the Nation's 8th-, 10th-, and 12th-graders, heroin use remained stable from 2003 to 2004. Lifetime heroin use measured 1.6 percent among 8th-graders and 1.5 percent among 10th- and 12th-graders.

The 2002 Drug Abuse Warning Network (DAWN), which collects data on drug-related hospital emergency department (ED) episodes from 21 metropolitan areas, reported that in 2002, heroin-related ED episodes numbered 93,519.

NIDA's Community Epidemiology Work Group (CEWG), which provides information about the nature and patterns of drug use in 21 areas, reported in its December 2003 publication that heroin was mentioned as the primary drug of abuse for large portions of drug abuse treatment admissions in Baltimore, Boston,

Detroit, Los Angeles, Newark, New York, and San Francisco.

## How is heroin used?

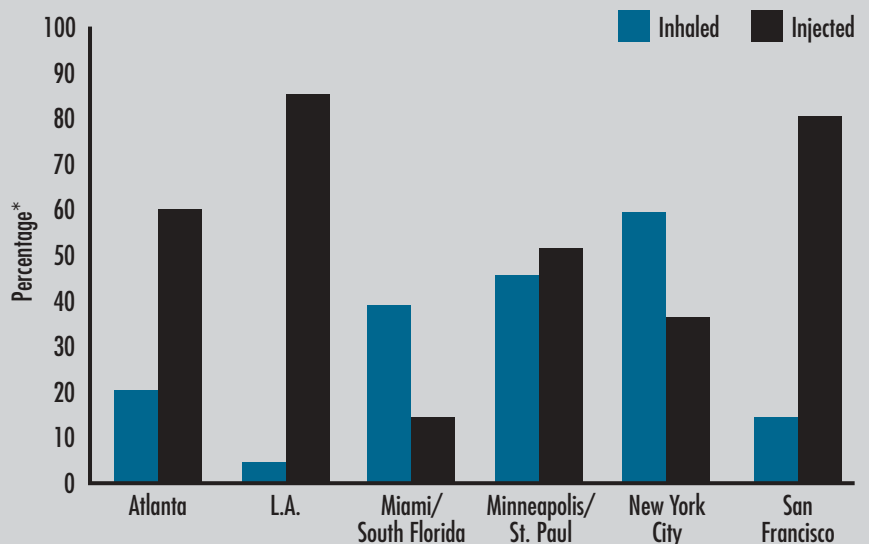
**H**eroin is usually injected, sniffed/snorted, or smoked. Typically, a heroin abuser may inject up to four times a day. Intravenous injection provides the greatest intensity and most rapid onset of euphoria (7 to 8 seconds), while intramuscular injection produces a relatively slow onset of euphoria (5 to 8 minutes). When heroin is sniffed or smoked, peak effects are usually felt within 10 to 15 minutes. NIDA researchers have confirmed that all forms of heroin administration are addictive.

Injection continues to be the predominant method of

heroin use among addicted users seeking treatment; in many CEWG areas, heroin injection is reportedly on the rise, while heroin inhalation is declining. However, certain groups, such as White suburbanites in the Denver area, report smoking or inhaling heroin because they believe that these routes of administration are less likely to lead to addiction.

With the shift in heroin abuse patterns comes an even more diverse group of users. In recent years, the availability of higher purity heroin (which is more suitable for inhalation) and the decreases in prices reported in many areas have increased the appeal of heroin for new users who are reluctant to inject. Heroin has also been appearing in more affluent communities.

### Route of Administration Among Heroin Treatment Admissions in Selected Areas



Source: Community Epidemiology Work Group, NIDA, December 2003, Vol. II.  
\*Includes first half 2003 data from treatment facilities.

## Opiates Act on Many Places in the Brain and Nervous System

- *Opiates can depress breathing by changing neurochemical activity in the brain stem, where automatic body functions are controlled.*

- *Opiates can change the limbic system, which controls emotions, to increase feelings of pleasure.*

- *Opiates can block pain messages transmitted through the spinal cord from the body.*

## What are the immediate (short-term) effects of heroin use?

Soon after injection (or inhalation), heroin crosses the blood–brain barrier. In the brain, heroin is converted to morphine and binds rapidly to opioid receptors. Abusers typically report feeling a surge of pleasurable sensation—a “rush.” The intensity of the rush is a function of how much drug is taken and how rapidly the drug enters the brain and binds to the natural opioid receptors. Heroin is particularly addictive because

it enters the brain so rapidly. With heroin, the rush is usually accompanied by a warm flushing of the skin, dry mouth, and a heavy feeling in the extremities, which may be accompanied by nausea, vomiting, and severe itching.

After the initial effects, abusers usually will be drowsy for several hours. Mental function is clouded by heroin’s effect on the central nervous system. Cardiac function slows. Breathing is also severely slowed, sometimes to the point of death. Heroin overdose is a particular risk on the street, where the amount and purity of the drug cannot be accurately known.

## What are the long-term effects of heroin use?

One of the most detrimental long-term effects of heroin use is addiction itself. Addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use, and by neurochemical and molecular changes in the brain. Heroin also produces profound degrees of tolerance and physical dependence, which are also powerful motivating factors for compulsive use and abuse. As with abusers of any addictive drug, heroin abusers gradually spend more and more time and energy obtaining and using the drug. Once they are addicted, the heroin abusers’ primary purpose in life becomes seeking and using drugs. The drugs literally change their brains and their behavior.

Physical dependence develops with higher doses of the drug. With physical dependence, the body adapts to the presence of the drug and withdrawal symptoms occur if use is reduced abruptly. Withdrawal may occur within a few hours after the last time the drug is taken. Symptoms of withdrawal include restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps (“cold turkey”), and leg movements. Major withdrawal symptoms peak between 24 and 48 hours after the last dose of heroin and subside after about a week. However, some people

have shown persistent withdrawal signs for many months. Heroin withdrawal is never fatal to otherwise healthy adults, but it can cause death to the fetus of a pregnant addict.

At some point during continuous heroin use, a person can become addicted to the drug. Sometimes addicted individuals will endure many of the withdrawal symptoms to reduce their tolerance for the drug so that they can again experience the rush.

Physical dependence and the emergence of withdrawal symptoms were once believed to be the key features of heroin addiction. We now know this may not be the case entirely, since craving and relapse can occur weeks and months after withdrawal symptoms are long gone. We also know that patients with chronic pain who need opiates to function (sometimes over extended periods) have few if any problems leaving opiates after their pain is resolved by

other means. This may be because the patient in pain is simply seeking relief of pain and not the rush sought by the addict.

## What are the medical complications of chronic heroin use?

**M**edical consequences of chronic heroin injection use include scarred and/or collapsed veins, bacterial infections of the blood vessels and heart valves, abscesses (boils) and other soft-tissue infections, and liver or kidney disease. Lung complications (including various types of pneumonia and tuberculosis) may result from the poor health condition of the abuser as well as from heroin's depressing effects on respiration. Many of the additives in street heroin may include substances that do not readily dissolve and result in

clogging the blood vessels that lead to the lungs, liver, kidneys, or brain. This can cause infection or even death of small patches of cells in vital organs. Immune reactions to these or other contaminants can cause arthritis or other rheumatologic problems.

Of course, sharing of injection equipment or fluids can lead to some of the most severe consequences of heroin abuse— infections with hepatitis B and C, HIV, and a host of other blood-borne viruses, which drug abusers can then pass on to their sexual partners and children.

## How does heroin abuse affect pregnant women?

**H**eroin abuse during pregnancy and its many associated environmental factors (e.g., lack of prenatal care) have been associated with adverse consequences including low birth weight, an important risk factor for later developmental delay. Methadone maintenance combined with prenatal care and a comprehensive drug treatment program can improve many of the detrimental maternal and neonatal outcomes associated with untreated heroin abuse, although infants exposed to methadone during pregnancy typically require treatment for withdrawal symptoms. In the United States, several studies have found buprenorphine to be equally effective and as safe as methadone in the adult outpatient treatment of opioid dependence. Given this efficacy

### Short- and Long-Term Effects of Heroin Abuse

#### Short-Term Effects:

- "Rush"
- Depressed respiration
- Clouded mental functioning
- Nausea and vomiting
- Suppression of pain
- Spontaneous abortion

#### Long-Term Effects:

- Addiction
- Infectious diseases, for example, HIV/AIDS and hepatitis B and C
- Collapsed veins
- Bacterial infections
- Abscesses
- Infection of heart lining and valves
- Arthritis and other rheumatologic problems



## NIDA National Drug Abuse Treatment Clinical Trials Network

[drugabuse.gov/CTN](http://drugabuse.gov/CTN)

States highlighted currently have CTN Nodes in place.

among adults, current studies are attempting to establish the safety and effectiveness of buprenorphine in opioid-dependent pregnant women. For women who do not want or are not able to receive pharmacotherapy for their heroin addiction, detoxification from opiates during pregnancy can be accomplished with relative safety, although the likelihood of relapse to heroin use should be considered.

### Why are heroin users at special risk for contracting HIV/AIDS and hepatitis B and C?

**H**eroin users are at risk for contracting HIV, hepatitis C (HCV), and other infectious diseases, through sharing and reuse of syringes and injection paraphernalia that have been used by infected individuals, or through unprotected sexual contact with an infected person.

Injection drug users (IDUs) represent the highest risk group for acquiring HCV infection; an estimated 70 to 80 percent of the 35,000 new HCV infections occurring in the United States each year are among IDUs.

NIDA-funded research has found that drug abusers can change the behaviors that put them at risk for contracting HIV through drug abuse treatment, prevention, and community-based outreach programs. They can eliminate drug use, drug-related risk behaviors such as needle sharing, unsafe sexual practices, and, in turn, the risk of exposure to HIV/AIDS and other infectious diseases. Drug abuse prevention and treatment are highly effective in preventing the spread of HIV.

### What are the treatments for heroin addiction?

**A** variety of effective treatments are available for heroin addiction. Treatment

tends to be more effective when heroin abuse is identified early. The treatments that follow vary depending on the individual, but methadone, a synthetic opiate that blocks the effects of heroin and eliminates withdrawal symptoms, has a proven record of success for people addicted to heroin. Other pharmaceutical approaches, such as buprenorphine, and many behavioral therapies also are used for treating heroin addiction. Buprenorphine is a recent addition to the array of medications now available for treating addiction to heroin and other opiates. This medication is different from methadone in that it offers less risk of addiction and can be prescribed in the privacy of a doctor's office. Buprenorphine/naloxone (Suboxone) is a combination drug product formulated to minimize abuse.

### Detoxification

Detoxification programs aim to achieve safe and humane withdrawal from opiates by minimizing the severity of withdrawal symptoms and other medical complications. The primary objective of detoxification is to relieve withdrawal symptoms while patients adjust to a drug-free state. Not in itself a treatment for addiction, detoxification is a useful step only when it leads into long-term treatment that is either drug-free (residential or outpatient) or uses medications as part of the treatment. The best documented drug-free treatments are the therapeutic community residential programs lasting 3 to 6 months.

Opiate withdrawal is rarely fatal. It is characterized by acute

## Buprenorphine

Name \_\_\_\_\_ Date \_\_\_\_\_  
Address \_\_\_\_\_



### A New Medication for Treating Opiate Addiction

- First medication developed to treat opiate addiction in the privacy of a physician's office.
- Binds to same receptors as morphine, but does not produce the same effects.
- Offers a valuable tool for physicians in treating the nearly 900,000 chronic heroin users in the U.S.
- As of March 2004, 3,951 U.S. physicians were eligible to prescribe buprenorphine to patients.

### The Story of Discovery

- First synthesized as an analgesic in England, 1969.
- Recognized as a potential addiction treatment by NIDA researchers in the 1970s.
- NIDA created Medications Development Division to focus on developing drug treatments for addiction, 1990.
- NIDA formed an agreement with the original developer to bring buprenorphine to market in the U.S., 1994.
- Buprenorphine tablets approved by the FDA, 2002.

withdrawal symptoms which peak 48 to 72 hours after the last opiate dose and disappear within 7 to 10 days, to be followed by a longer term abstinence syndrome of general malaise and opioid craving.

### Methadone programs

Methadone treatment has been used for more than 30 years to effectively and safely treat opioid addiction. Properly prescribed methadone is not intoxicating or sedating, and its effects do not interfere with ordinary activities such as driving a car. The medication is taken orally and it suppresses narcotic withdrawal for 24 to 36 hours. Patients are able to perceive pain and

have emotional reactions. Most important, methadone relieves the craving associated with heroin addiction; craving is a major reason for relapse. Among methadone patients, it has been found that normal street doses of heroin are ineffective at producing euphoria, thus making the use of heroin more easily extinguishable.

Methadone's effects last four to six times as long as those of heroin, so people in treatment need to take it only once a day. Also, methadone is medically safe even when used continuously for 10 years or more. Combined with behavioral therapies or counseling and other supportive services, methadone enables

patients to stop using heroin (and other opiates) and return to more stable and productive lives. Methadone dosages must be carefully monitored in patients who are receiving antiviral therapy for HIV infection, to avoid potential medication interactions.

### Buprenorphine and other medications

Buprenorphine is a particularly attractive treatment for heroin addiction because, compared with other medications, such as methadone, it causes weaker opiate effects and is less likely to cause overdose problems. Buprenorphine also produces a lower level of physical dependence, so patients who discontinue the medication generally have fewer withdrawal symptoms than do those who stop taking methadone. Because of these advantages, buprenorphine may be appropriate for use in a wider variety of treatment settings than the currently available medications. Several other medications with potential for treating heroin overdose or addiction are currently under investigation by NIDA.

In addition to methadone and buprenorphine, other drugs aimed at reducing the severity of the withdrawal symptoms can be prescribed. Clonidine is of some benefit but its use is limited due to side effects of sedation and hypotension. Lofexidine, a centrally acting alpha-2 adrenergic agonist, was launched in 1992 specifically for symptomatic relief in patients undergoing opiate withdrawal. Naloxone and naltrexone are medications that also block the effects of

morphine, heroin, and other opiates. As antagonists, they are especially useful as antidotes. Naltrexone has long-lasting effects, ranging from 1 to 3 days, depending on the dose.

Naltrexone blocks the pleasurable effects of heroin and is useful in treating some highly motivated individuals. Naltrexone has also been found to be successful in preventing relapse by former opiate addicts released from prison on probation.

### Behavioral therapies

Although behavioral and pharmacologic treatments can be extremely useful when employed alone, science has taught us that integrating both types of treatments will ultimately be the most effective approach. There are many effective behavioral treatments available for heroin addiction. These can include residential and outpatient approaches. An important task is to match the best treatment approach to meet the particular needs of the patient. Moreover, several new behavioral therapies, such as contingency management therapy and cognitive-behavioral interventions, show particular promise as treatments for heroin addiction, especially when applied in concert with pharmacotherapies. Contingency management therapy uses a voucher-based system, where patients earn “points” based on negative drug tests, which they can exchange for items that encourage healthy living. Cognitive-behavioral interventions are designed to help modify the patient’s expectations and behaviors related to drug

use, and to increase skills in coping with various life stressors. Both behavioral and pharmacological treatments help to restore a degree of normalcy to brain function and behavior, with increased employment rates and lower risk of HIV and other diseases and criminal behavior.

### What are the opioid analogs and their dangers?

**D**rug analogs are chemical compounds that are similar to other drugs in their effects but differ slightly in their chemical structure. Some analogs are produced by pharmaceutical companies for legitimate medical reasons. Other analogs, sometimes referred to as “designer” drugs, can be produced in illegal laboratories and are often more dangerous and potent than the original drug. Two of the most commonly known opioid analogs are fentanyl and meperidine (marketed under the brand name Demerol, for example).

Fentanyl was introduced in 1968 by a Belgian pharmaceutical company as a synthetic narcotic to be used as an analgesic in surgical procedures because of its minimal effects on the heart. Fentanyl is particularly dangerous because it is 50 times more potent than heroin and can rapidly stop respiration. This is not a problem during surgical procedures because machines are used to help patients breathe. On the street, however, users have been found dead with the needle used to inject the drug still in his or her arm.

### Where can I get further scientific information about heroin abuse and addiction?

**T**o learn more about heroin and other drugs of abuse, contact the National Clearinghouse for Alcohol and Drug Information (NCADI) at 1-800-729-6686. Information specialists are available to help you locate information and resources.

Fact sheets, including *InfoFacts*, on the health effects of heroin, other drugs of abuse, and other drug abuse topics are available on the NIDA Web site ([www.drugabuse.gov](http://www.drugabuse.gov)), and can be ordered free of charge in English and Spanish from NCADI at [www.health.org](http://www.health.org).

#### Access information on the Internet

- What’s new on the NIDA Web site
- Information on drugs of abuse
- Publications and communications (including *NIDA NOTES*)
- Information on clinical trials through CTN
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

#### NIDA Web Sites

[www.drugabuse.gov](http://www.drugabuse.gov)  
[www.drugabuse.gov/CTN](http://www.drugabuse.gov/CTN)

#### NCADI

Web Site: [www.health.org](http://www.health.org)  
 Phone No.: 1-800-729-6686

## Glossary

**Addiction:** A chronic, relapsing disease, characterized by compulsive drug seeking and use and by neurochemical and molecular changes in the brain.

**Agonist:** A chemical compound that mimics the action of a natural neurotransmitter to produce a biological response.

**Analog:** A chemical compound that is similar to another drug in its effects but differs slightly in its chemical structure.

**Antagonist:** A drug that counteracts or blocks the effects of another drug.

**Buprenorphine:** A mixed opiate agonist/antagonist medication for the treatment of heroin addiction.

**Craving:** A powerful, often uncontrollable desire for drugs.

**Detoxification:** A process of allowing the body to rid itself of a drug while managing the symptoms of withdrawal; often the first step in a drug treatment program.

**Fentanyl:** A medically useful opioid analog that is 50 times more potent than heroin.

**Meperidine:** A medically approved opioid available under various brand names (e.g., Demerol).

**Methadone:** A long-acting synthetic medication shown to be effective in treating heroin addiction.

**Physical dependence:** An adaptive physiological state that occurs with regular drug use and results in a withdrawal syndrome when drug use is stopped; usually occurs with tolerance.

**Rush:** A surge of euphoric pleasure that rapidly follows administration of a drug.

**Tolerance:** A condition in which higher doses of a drug are required to produce the same effect as during initial use; often leads to physical dependence.

**Withdrawal:** A variety of symptoms that occur after use of an addictive drug is reduced or stopped.

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ON DRUG ABUSE

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How does marijuana use affect school, work, and social life? See page 7.

## Research Report Series

### from the director:

By the time they graduate from high school, about 42 percent of teens will have tried marijuana. Although current use among U.S. teens has dropped dramatically in the past decade (to a prevalence of about 14 percent in 2009), this decline has stalled during the past several years. These data are from the Monitoring the Future study, which has been tracking drug use among teens since 1975. Still, the World Health Organization ranks the United States first among 17 European and North American countries for prevalence of marijuana use. And more users start every day. In 2008, an estimated 2.2 million Americans used marijuana for the first time; greater than half were under age 18.

The use of marijuana can produce adverse physical, mental, emotional, and behavioral effects. It can impair short-term memory and judgment and distort perception. Because marijuana affects brain systems that are still maturing through young adulthood, its use by teens may have a negative effect on their development. And contrary to popular belief, it can be addictive.

We hope that this *Research Report* will help make readers aware of our current knowledge of marijuana abuse and its harmful effects.

Nora D. Volkow, M.D.  
Director  
National Institute on Drug Abuse

# Marijuana Abuse

## What Is Marijuana?

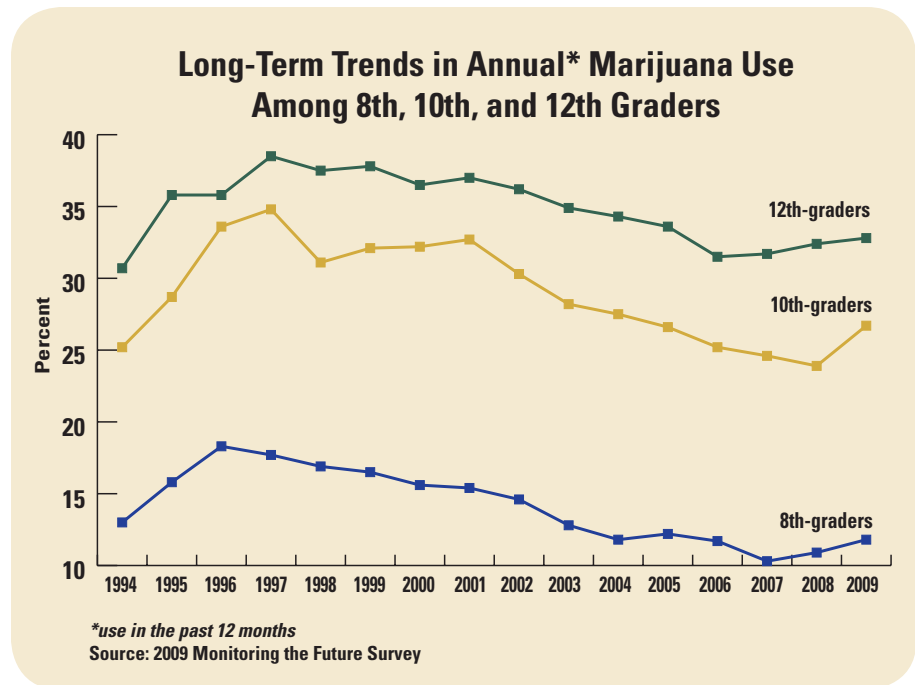
**M**arijuana—often called *pot*, *grass*, *reefer*, *weed*, *herb*, *Mary Jane*, or *MJ*—is a greenish-gray mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis sativa*—the hemp plant. Most users smoke marijuana in hand-rolled cigarettes called *joints*, among other names; some use pipes or water pipes called *bongs*. Marijuana cigars, or *blunts*, are also popular. To make blunts, users slice open cigars, remove some of the tobacco, and mix the remainder with marijuana (Timberlake 2009). Marijuana also is used to brew tea and sometimes is mixed into foods.

*continued inside*

## What Is the Scope of Marijuana Use in the United States?

Marijuana is the most commonly used illicit drug (15.2 million past-month users) according to the 2008 National Survey on Drug Use and Health (NSDUH). That year, marijuana was used by 75.6 percent of current illicit drug users (defined as having used the drug some time in the 30 days before the survey) and was the *only* drug used by 53.3 percent of them.

Marijuana use is widespread among adolescents and young adults. According to the Monitoring the Future Survey—an annual survey of attitudes and drug use among the Nation’s middle and high school students—most measures of marijuana use decreased

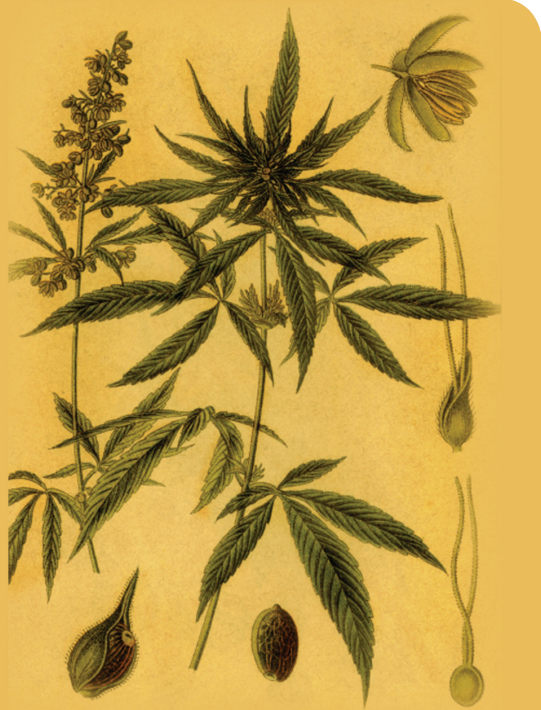


in the past decade among 8th-, 10th-, and 12th-graders. However, this decline has stalled in the past few years as attitudes have softened about marijuana’s risks. In 2009, 11.8 percent of 8th-graders reported marijuana use in the past year, and 6.5 percent were current users. Among 10th-graders, 26.7 percent had used marijuana in the past year, and 15.9 percent were current users. Rates of use among 12th-graders were higher still: 32.8 percent had used marijuana during the year prior to the survey, and 20.6 percent were current users.

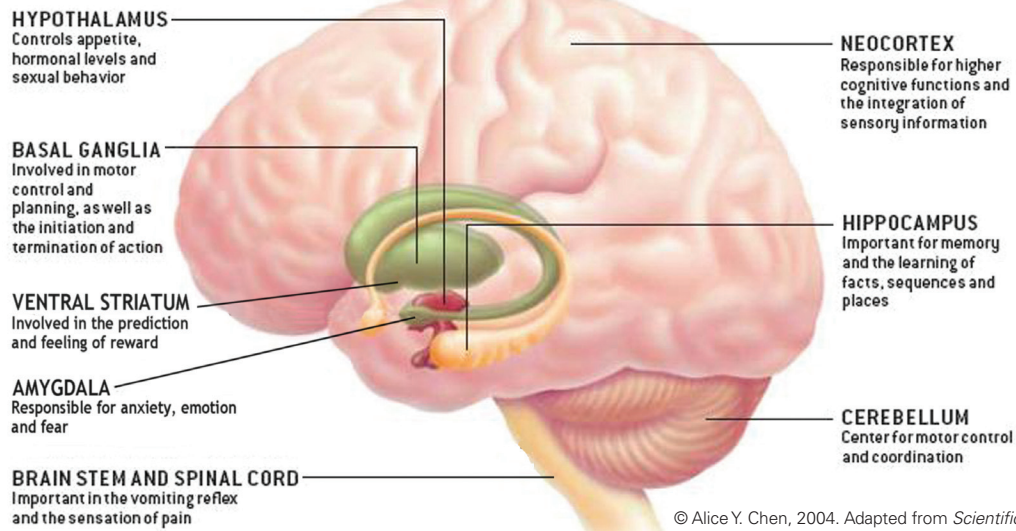
The Drug Abuse Warning Network (DAWN), a system for monitoring the health impact of drugs, estimated that in 2008, marijuana was a contributing factor in over 374,000 emergency department (ED) visits in the United States, with about two-thirds of patients being male, and 13 percent between the ages of 12 and 17.

## How Does Marijuana Produce its Effects?

Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in marijuana, responsible for many of its known effects. When marijuana is smoked, its effects begin almost immediately. THC rapidly passes from the lungs into the bloodstream, which carries the chemical to organs throughout the body, including the brain. The effects of smoked marijuana can last from 1 to 3 hours. If marijuana is consumed in foods or beverages, the effects appear later—usually in 30 minutes to 1 hour—but can last up to 4 hours. Smoking marijuana delivers significantly more THC into the bloodstream than eating or drinking the drug.



## Marijuana's Effects on the Brain



When marijuana is smoked, its active ingredient, THC, travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.

Scientists have learned a great deal about how THC acts in the brain. THC binds to specific sites called *cannabinoid receptors* (CBRs) located on the surface of nerve cells. These receptors are found in high-density in areas of the brain that influence pleasure, memory, thinking, concentration, movement, coordination, and sensory and time perception. CBRs are part of a vast communication network known as the endocannabinoid system, which plays a critical role in normal brain development and function. In fact, THC effects are similar to those produced by naturally occurring chemicals found in the brain (and body) called *endogenous cannabinoids*. These chemicals help control many of the same mental and physical functions that may be disrupted by marijuana use.

When someone smokes marijuana, THC stimulates the CBRs artificially, disrupting

function of the natural, or endogenous, cannabinoids. An overstimulation of these receptors in key brain areas produces the marijuana “high,” as well as other effects on mental processes. Over time, this overstimulation can alter the function of CBRs, which, along with other changes in the brain, can lead to addiction and to withdrawal symptoms when drug use stops.

The THC content or potency of marijuana, as detected in confiscated samples over the past 30+ years (Potency Monitoring Project, University of Mississippi), has been steadily increasing. This increase raises concerns that the consequences of marijuana use could be worse than in the past, particularly among new users, or in young people, whose brains are still developing. We still do not know, however, whether cannabis users adjust for the increase in potency by using less or by smoking it differently. We also do not know

all the consequences to the brain and body when exposed to higher concentrations of THC.

## How Does Marijuana Use Affect Your Brain and Body?

### Effects on the Brain

As THC enters the brain, it causes the user to feel euphoric—or high—by acting on the brain’s reward system, which is made up of regions that govern the response to pleasurable things like sex and chocolate, as well as to most drugs of abuse. THC activates the reward system in the same way that nearly all drugs of abuse do: by stimulating brain cells to release the chemical dopamine.

Along with euphoria, relaxation is another frequently reported effect in human studies. Other effects, which vary dramati-

## ***Marijuana users who have taken large doses of the drug may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity.***

cally among different users, include heightened sensory perception (e.g., brighter colors), laughter, altered perception of time, and increased appetite. After a while, the euphoria subsides, and the user may feel sleepy or depressed. Occasionally, marijuana use may produce anxiety, fear, distrust, or panic.

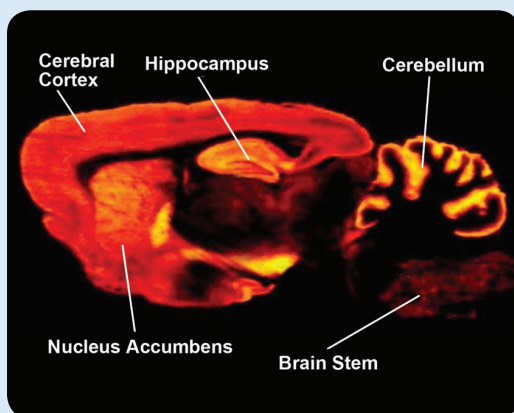
Marijuana use impairs a person's ability to form new memories (see below, “**Marijuana, Memory, and the Hippocampus**”) and to shift focus. THC also disrupts coordination and balance by binding to receptors in the cerebellum and basal ganglia—parts of the brain that regulate balance, posture, coordination, and reaction time. Therefore, learning, doing complicated tasks, participating in athletics, and driving are also affected.

Marijuana users who have taken large doses of the drug may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity. Although the specific causes of these symptoms remain unknown, they appear to occur more frequently when a high dose of cannabis is consumed in food or drink rather than smoked. Such short-term psychotic reactions to high concentrations of THC are distinct from longer-lasting, schizophrenia-like disorders that have been associated with the use of cannabis in vulnerable individuals. (See section on the link between marijuana use and mental illness, page 6.)

Our understanding of marijuana's long-term brain effects is limited. Research findings on how

chronic cannabis use affects brain *structure*, for example, have been inconsistent. It may be that the effects are too subtle for reliable detection by current techniques. A similar challenge arises in studies of the effects of chronic marijuana use on brain *function*. Although imaging studies (functional MRI; fMRI) in chronic users do show some consistent alterations, the relation of these changes to cognitive functioning is less clear. This uncertainty may stem from confounding factors such as other drug use, residual drug effects (which can occur for at least 24 hours in chronic users), or withdrawal symptoms in long-term chronic users.

An enduring question in the field is whether individuals who quit marijuana, even after long-term, heavy use, can recover some



Distribution of cannabinoid receptors in the rat brain. Brain image reveals high levels (shown in orange and yellow) of cannabinoid receptors in many areas, including the cortex, hippocampus, cerebellum, and nucleus accumbens (ventral striatum).

### **Marijuana, Memory, and the Hippocampus**

Memory impairment from marijuana use occurs because THC alters how information is processed in the hippocampus, a brain area responsible for memory formation.

Most of the evidence supporting this assertion comes from animal studies. For example, rats exposed to THC in utero, soon after birth, or during adolescence, show notable problems with specific learning/memory tasks later in life. Moreover, cognitive impairment in adult rats is associated with structural and func-

tional changes in the hippocampus from THC exposure during adolescence.

As people age, they lose neurons in the hippocampus, which decreases their ability to learn new information. Chronic THC exposure may hasten age-related loss of hippocampal neurons. In one study, rats exposed to THC every day for 8 months (approximately 30 percent of their lifespan) showed a level of nerve cell loss (at 11 to 12 months of age) that equaled that of unexposed animals twice their age.



of their cognitive abilities. One study reports that the ability of long-term heavy marijuana users to recall words from a list was still impaired 1 week after they quit using, but returned to normal by 4 weeks. However, another study found that marijuana's effects on the brain can build up and deteriorate critical life skills over time. Such effects may be worse in those with other mental disorders, or simply by virtue of the normal aging process.

### Effects on General Physical Health

Within a few minutes after inhaling marijuana smoke, an individual's heart rate speeds up, the bronchial passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look red. The heart rate—normally 70 to 80 beats per minute—may increase by 20 to 50 beats per minute, or may even double in some cases. Taking other drugs with marijuana can amplify this effect.

Limited evidence suggests that a person's risk of heart attack during the first hour after smoking marijuana is four times his or her usual risk. This observation could be partly explained by marijuana raising blood pressure (in some cases) and heart rate and reducing the blood's capacity to carry oxygen. Such possibilities need to be examined more closely, particularly since current marijuana users include adults from the baby

## Consequences of Marijuana Abuse

### Acute (present during intoxication)

- Impairs short-term memory
- Impairs attention, judgment, and other cognitive functions
- Impairs coordination and balance
- Increases heart rate
- Psychotic episodes

### Persistent (lasting longer than intoxication, but may not be permanent)

- Impairs memory and learning skills
- Sleep impairment

### Long-term (cumulative effects of chronic abuse)

- Can lead to addiction
- Increases risk of chronic cough, bronchitis
- Increases risk of schizophrenia in vulnerable individuals
- May increase risk of anxiety, depression, and amotivational syndrome\*

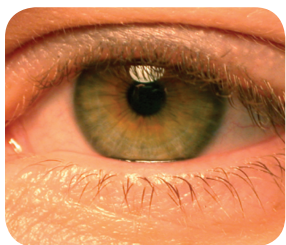
\*These are often reported co-occurring symptoms/disorders with chronic marijuana use. However, research has not yet determined whether marijuana is causal or just associated with these mental problems.

boomer generation, who may have other cardiovascular risks that may increase their vulnerability.

The smoke of marijuana, like that of tobacco, consists of a toxic mixture of gases and particulates, many of which are known to be harmful to the lungs. Someone who smokes marijuana regularly may have many of the same respiratory problems that tobacco smokers do, such as daily cough and phlegm production, more frequent acute chest illnesses, and a greater risk of lung infections.

Even infrequent marijuana use can cause burning and stinging of the mouth and throat, often accompanied by a heavy cough. One study found that extra sick days used by frequent marijuana smokers were often because of respiratory illnesses (Polen et al. 1993).

In addition, marijuana has the *potential* to promote cancer of the lungs and other parts of the respiratory tract because it contains irritants and carcinogens—up to 70 percent more than tobacco smoke. It also induces high levels



***Within a few minutes after inhaling marijuana smoke, an individual's heart rate speeds up, the bronchial passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look red.***

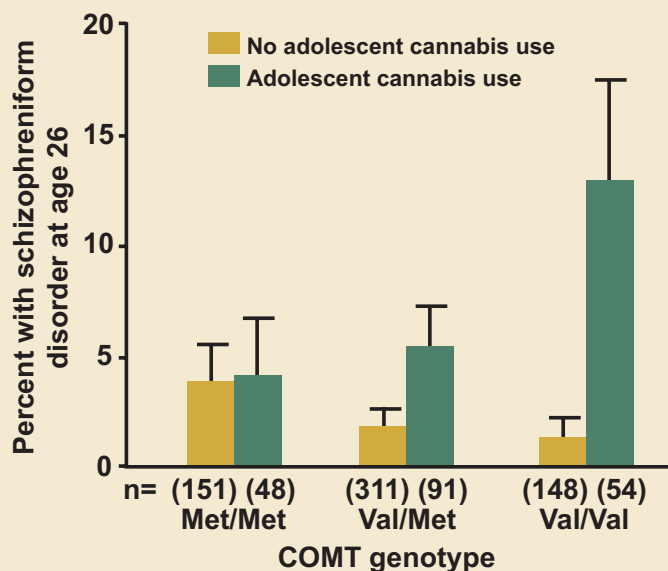
of an enzyme that converts certain hydrocarbons into their cancer-causing form, which could accelerate the changes that ultimately produce malignant cells. And since marijuana smokers generally inhale more deeply and hold their breath longer than tobacco smokers, the lungs are exposed longer to carcinogenic smoke. However, while several lines of evidence have suggested that marijuana use may lead to lung cancer, the supporting evidence is inconclusive (Hashibe et al. 2006). The presence of an

unidentified active ingredient in cannabis smoke having protective properties—if corroborated and properly characterized—could help explain the inconsistencies and modest findings.

A significant body of research demonstrates negative effects of THC on the function of various immune cells, both in vitro in cells and in vivo with test animals. However, no studies to date connect marijuana’s suspected immune system suppression with greater incidence of infections or immune

disorders in humans. One short (3-week) study found marijuana smoking to be associated with a few statistically significant negative effects on the immune function of AIDS patients; a second small study of college students also suggested the possibility of marijuana having adverse effects on immune system functioning. Thus, the combined evidence from animal studies plus the limited human data available, seem to warrant additional research on the impact of marijuana on the immune system. (See also “The Science of Medical Marijuana,” page 9.)

### Genetic variation in COMT influences the harmful effects of abused drugs



Adapted from Caspi et al., *Biol Psychiatry*, May 2005.

*The influence of adolescent marijuana use on adult psychosis is affected by genetic variables. This figure shows that variations in a gene can affect the likelihood of developing psychosis in adulthood, following exposure to cannabis in adolescence. The COMT gene governs an enzyme that breaks down dopamine, a brain chemical involved in schizophrenia. It comes in two forms: “Met” and “Val.” Individuals with one or two copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence (dark bars). Those with only the Met variant were unaffected by cannabis use.*

## Is There a Link Between Marijuana Use and Mental Illness?

Research in the past decade has focused on whether marijuana use actually causes other mental illnesses. The strongest evidence to date suggests a link between cannabis use and psychosis (Hall and Degenhardt 2009). For example, a series of large prospective studies that followed a group of people over time showed a relationship between marijuana use and later development of psychosis. Marijuana use also worsens the course of illness in patients with schizophrenia and can produce a brief psychotic reaction in some users that fades as the drug wears off. The amount of drug used, the age at first use, and genetic vulnerability can all influence this relationship. One example is a study (illustrated, page

6) that found an increased risk of psychosis among adults who had used marijuana in adolescence *and* who also carried a specific variant of the gene for catechol-O-methyltransferase (COMT) (Caspi et al. 2005), an enzyme that degrades neurotransmitters such as dopamine and norepinephrine.

In addition to the observed links between marijuana use and schizophrenia, other less consistent associations have been reported between marijuana use and depression, anxiety, suicidal thoughts among adolescents, and personality disturbances. One of the most frequently cited, albeit still controversial, is an amotivational syndrome, defined as a diminished or absent drive to engage in typically rewarding activities. Because of the role of the endocannabinoid system in regulating mood, these associations make a certain amount of sense; however, more research is needed to confirm and better understand these linkages.

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## Is Marijuana Addictive?

Long-term marijuana use can lead to addiction; that is, people have difficulty controlling their drug use and cannot stop even though it interferes with many aspects of their lives. It is estimated that 9 percent of people who use marijuana will become dependent on it. The number goes up to about 1 in 6 in those who start using young (in their teens) and to 25–50 percent among daily users. Moreover, a study of over 300 fraternal and identical twin pairs



found that the twin who had used marijuana before the age of 17 had elevated rates of other drug use and drug problems later on, compared with their twin who did not use before age 17.

According to the 2008 NSDUH, marijuana accounted for 4.2 million of the estimated 7 million Americans dependent on or abusing illicit drugs. In 2008, approximately 15 percent of people entering drug abuse treatment programs reported marijuana as their primary drug of abuse; 61 percent of persons under 15 reported marijuana as their primary drug of abuse, as did 56 percent of those 15 to 19 years old.

Marijuana addiction is also linked to a withdrawal syndrome similar to that of nicotine withdrawal, which can make it hard to quit. People trying to quit report irritability, sleeping difficulties, craving, and anxiety. They also show increased aggression on psychological tests, peaking approximately 1 week after they last used the drug.

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## How Does Marijuana Use Affect School, Work, and Social Life?

Research has shown that marijuana's negative effects on attention, memory, and learning can last for days or weeks after the acute effects of the drug wear off (Schweinsburg et al. 2008). Consequently, someone who smokes marijuana daily may be functioning at a reduced intellectual level most or all of the time. Not surprisingly, evidence suggests that, compared with their nonsmoking peers, students who smoke marijuana tend to get lower grades and are more likely to drop out of high school (Fergusson and Boden 2008). A meta-analysis of 48 relevant studies—one of the most thorough performed to date—found cannabis use to be associated consistently with reduced educational attainment (e.g., grades and chances of graduating) (Macleod et al. 2004). However, a *causal* relationship is not yet proven between cannabis use by young people and psychosocial harm.

That said, marijuana users themselves report poor outcomes on a variety of life satisfaction and achievement measures. One study compared current and former long-term heavy users of marijuana with a control group who reported smoking cannabis at least once in their lives but not more than 50 times. Despite similar education and income backgrounds, significant differences were found in educational attainment: fewer of the heavy users of cannabis com-

pleted college, and more had yearly household incomes of less than \$30,000. When asked how marijuana affected their cognitive abilities, career achievements, social lives, and physical and mental health, the majority of heavy cannabis users reported the drug's negative effects on all of these measures. In addition, several studies have linked workers' marijuana smoking with increased absences, tardiness, accidents, workers' compensation claims, and job turnover. For example, a study among postal workers found that employees who tested positive for marijuana on a pre-employment urine drug test had 55 percent more industrial accidents, 85 percent more injuries, and a 75-percent increase in absenteeism compared with those who tested negative for marijuana use.

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## Does Marijuana Use Affect Driving?

Because marijuana impairs judgment and motor coordination and slows reaction time, an intoxicated person has an increased chance of being involved in and being responsible for an accident (O'Malley



and Johnston 2007; Richer and Bergeron 2009). According to the National Highway Traffic Safety Administration, drugs other than alcohol (e.g., marijuana and cocaine) are involved in about 18 percent of motor vehicle driver deaths. A recent survey found that 6.8 percent of drivers, mostly under 35, who were involved in accidents tested positive for THC; alcohol levels above the legal limit were found in 21 percent of such drivers.

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## Can Marijuana Use During Pregnancy Harm the Baby?

Animal research suggests that the body's endocannabinoid system plays a role in the control of brain maturation, particularly in the development of emotional responses. It is conceivable that even low concentrations of THC, when administered during the perinatal period, could have profound and long-lasting consequences for both brain and behavior (Trezza et al. 2008). Research has shown that some babies born to women who used marijuana during their pregnancies display altered responses to visual stimuli, increased tremulousness, and a high-pitched cry, which could indicate problems with neurological development. In school, marijuana-exposed children are more likely to show gaps in problemsolving skills, memory, and the ability to remain attentive. More research is needed, however, to disentangle

the drug-specific factors from the environmental ones (Schempf and Strobino 2008).

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## Available Treatments for Marijuana Use Disorders

Marijuana dependence appears to be very similar to other substance dependence disorders, although the long-term clinical outcomes may be less severe. On average, adults seeking treatment for marijuana abuse or dependence have used marijuana nearly every day for more than 10 years and have attempted to quit more than six times. It is important to note that marijuana dependence is most prevalent among patients suffering from other psychiatric disorders, particularly among adolescent and young adult populations (Gouzoulis-Mayfrank 2008). Also, marijuana abuse or dependence typically co-occurs with use of other drugs, such as cocaine and alcohol. Available studies indicate that effectively treating the mental health disorder with standard treatments involving medications and behavioral therapies may help reduce cannabis use, particularly among heavy users and those with more chronic mental disorders. Behavioral treatments, such as motivational enhancement therapy (MET), group or individual cognitive-behavioral therapy (CBT), and contingency management (CM), as well as family-based treatments, have shown promise.

Unfortunately, the success rates of treatment are rather modest. Even with the most effective treatment for adults, only about 50 percent of enrollees achieve an initial 2-week period of abstinence, and among those who do, approximately half will resume use within a year. Across studies, 1-year abstinence rates have ranged between 10 and 30 percent for the various behavioral approaches. As with other addictions, these data suggest that a chronic care model should be considered for marijuana addiction, with treatment intensity stepped up or down based on need, comorbid addictions or other mental disorders, and the availability of family and other supports.

Currently, no medications are available to treat marijuana abuse, but research is active in this area. Most of the studies to date have targeted the marijuana withdrawal syndrome. For example, a recent human laboratory study showed that a combination of a cannabinoid agonist medication with lofexidine (a medication approved in the United Kingdom for the treatment of opioid withdrawal) produced more robust improvements in sleep and decreased marijuana withdrawal, craving, and relapse in daily marijuana smokers relative to either medication alone. Recent discoveries about the inner workings of the endogenous cannabinoid system raise the future possibility of a medication able to block THC's intoxicating effects, which could help prevent relapse by reducing or eliminating marijuana's appeal.

## The Science of Medical Marijuana



The potential medicinal properties of marijuana have been the subject of substantive research and heated debate. Scientists have confirmed that the cannabis plant contains active ingredients with therapeutic potential for relieving pain, controlling nausea, stimulating appetite, and decreasing ocular pressure. As a result, a 1990 Institute of Medicine report concluded that further clinical research on cannabinoid drugs and safe delivery systems was warranted.

At that time, dronabinol (Marinol®) and nabilone (Cesamet®) were the only FDA-approved, marijuana-based medications that doctors could prescribe for the treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS. These pills contained synthetic versions of THC, the main active ingredient in marijuana. Today, 25 years after their approval, the development of Sativex® marks the arrival of the second generation of cannabis-based medications. This new product (currently available in the United Kingdom and Canada) is a chemically pure mixture of plant-derived THC and Cannabidiol, formulated as a mouth spray and approved for the relief of cancer-associated pain and spasticity and neuropathic pain in multiple sclerosis.

Scientists continue to investigate the medicinal properties of THC and other cannabinoids to better evaluate and harness their ability to help patients suffering from a broad range of conditions, while avoiding the adverse effects of smoked marijuana. These efforts are bound to improve our understanding of the cannabinoid system and help us bring to market a new generation of safe and effective medications.

## Glossary

**Addiction:** A chronic, relapsing disease characterized by compulsive drug seeking and use and by long-lasting changes in the brain.

**Basal Ganglia:** Structures located deep in the brain that play an important role in the initiation of movements. These clusters of neurons include the caudate nucleus, putamen, globus pallidus, and substantia nigra. It also contains the nucleus accumbens, which is the main center of reward in the brain.

**Cerebellum:** A large structure located in the back of the brain that helps control the coordination of movement by making connections to other parts of the CNS (pons, medulla, spinal cord, and thalamus). It also may be involved in aspects of motor learning.

**Cerebral Cortex:** The outermost layer of the cerebral hemispheres of the brain. It is largely responsible for conscious experience, including perception, emotion, thought, and planning.

**Cannabinoids and Cannabinoid Receptors:** A family of chemicals that bind to specific (cannabinoid) receptors to influence mental and physical functions. Cannabinoids that are produced naturally by the body are referred to as endocannabinoids. They play important roles in development, memory, pain, appetite, among others. The marijuana plant (*Cannabis sativa*) contains delta-9-tetrahydrocannabinol (THC) that can disrupt these processes, if administered repeatedly and/or in high enough concentrations.

**Carcinogen:** Any substance that causes cancer.

**Cognitive-Behavioral Therapy (CBT):** A form of psychotherapy that teaches people strategies to identify and correct problematic behaviors in order to enhance self-control, stop drug use, and address a range of other problems that often co-occur with them.

**Contingency Management (CM):** A therapeutic management approach based on frequent monitoring of the target behavior and the provision (or removal) of tangible, positive rewards when the target behavior occurs (or does not). CM techniques have shown to be effective for keeping people in treatment and promoting abstinence.

**Dopamine:** A brain chemical, classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

**Hippocampus:** A seahorse-shaped structure located within the brain that is considered an important part of the limbic system. One of the most studied areas of the brain, the hippocampus plays key roles in learning, memory, and emotion.

**Hydrocarbon:** Any chemical compound containing only hydrogen and carbon.

**Motivational Enhancement Therapy (MET):** A systematic form of intervention designed to produce rapid, internally motivated change. MET does not attempt to treat the person, but rather mobilize their own internal resources for change and engagement in treatment.

**Psychosis:** A mental disorder (e.g., schizophrenia) characterized by delusional or disordered thinking detached from reality; symptoms often include hallucinations.

**Schizophrenia:** A psychotic disorder characterized by symptoms that fall into two categories: (1) positive symptoms, such as distortions in thoughts (delusions), perception (hallucinations), and language and thinking and (2) negative symptoms, such as flattened emotional responses and decreased goal-directed behavior.

**Schizophreniform Disorders:** Similar to schizophrenia, but of shorter duration and possibly lesser severity.

**THC:** Delta-9-tetrahydrocannabinol; the main active ingredient in marijuana, which acts on the brain to produce its effects.

**Ventral Striatum:** An area of the brain that is part of the basal ganglia and becomes activated and flooded with dopamine in the presence of salient stimuli. The release of this chemical also occurs during physically rewarding activities such as eating, sex, and taking drugs, and is a key factor behind our desire to repeat these activities.

**Withdrawal:** Adverse symptoms that occur after chronic use of a drug is reduced or stopped.

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## Where Can I Get More Scientific Information on Marijuana Abuse?

To learn more about marijuana and other drugs of abuse, or to order materials on these topics free of charge in English or Spanish, visit the NIDA Web site at [www.drugabuse.gov](http://www.drugabuse.gov) or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).



### What's New on the NIDA Web Site

- Information on drugs of abuse
- Publications and communications (including *NIDA Notes* and *Addiction Science & Clinical Practice journal*)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

### NIDA Web Sites

[drugabuse.gov](http://drugabuse.gov)  
[backtoschool.drugabuse.gov](http://backtoschool.drugabuse.gov)  
[marijuana-info.org](http://marijuana-info.org)  
[teens.drugabuse.gov](http://teens.drugabuse.gov)

### For Physician Information



[www.drugabuse.gov/nidamed](http://www.drugabuse.gov/nidamed)

### Other Web Sites

Information on marijuana abuse is also available through the following Web site:

- Substance Abuse and Mental Health Services Administration Health Information Network:  
[www.samhsa.gov/shin](http://www.samhsa.gov/shin)

## U.S. Department of Health and Human Services

NATIONAL INSTITUTES OF HEALTH

**NIDA** NATIONAL INSTITUTE  
ON DRUG ABUSE

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# Research Report

S E R I E S

*The abuse of methamphetamine—a potent and highly addictive psycho-stimulant—is a very serious problem in the United States. Initially limited to Hawaii and western parts of the country, methamphetamine abuse continues to spread eastward, with rural and urban areas everywhere increasingly affected. According to one national survey, approximately 10 million people in the United States have tried methamphetamine at least once.*

*Methamphetamine abuse leads to devastating medical, psychological, and social consequences. Adverse health effects include memory loss, aggression, psychotic behavior, heart damage, malnutrition, and severe dental problems. Methamphetamine abuse also contributes to increased transmission of infectious diseases, such as hepatitis and HIV/AIDS, and can infuse whole communities with new waves of crime, unemployment, child neglect or abuse, and other social ills.*

*The good news is that methamphetamine abuse can be prevented and methamphetamine addiction can be treated. People do recover, but only when effective treatments that address the multitude of problems resulting from methamphetamine abuse are readily available. Primary goals of the National Institute on Drug Abuse (NIDA) are to apply what our scientists learn from drug abuse research to develop new and enhance existing treatment approaches and to bring these effective treatments to the communities that need them.*

*In this report, we provide an overview of the latest scientific findings on methamphetamine. Our intent is to enlighten readers about the damaging effects of methamphetamine abuse and to inform prevention and treatment efforts.*

**Nora D. Volkow, M.D.**  
 Director  
 National Institute on Drug Abuse

from the director

## METHAMPHETAMINE

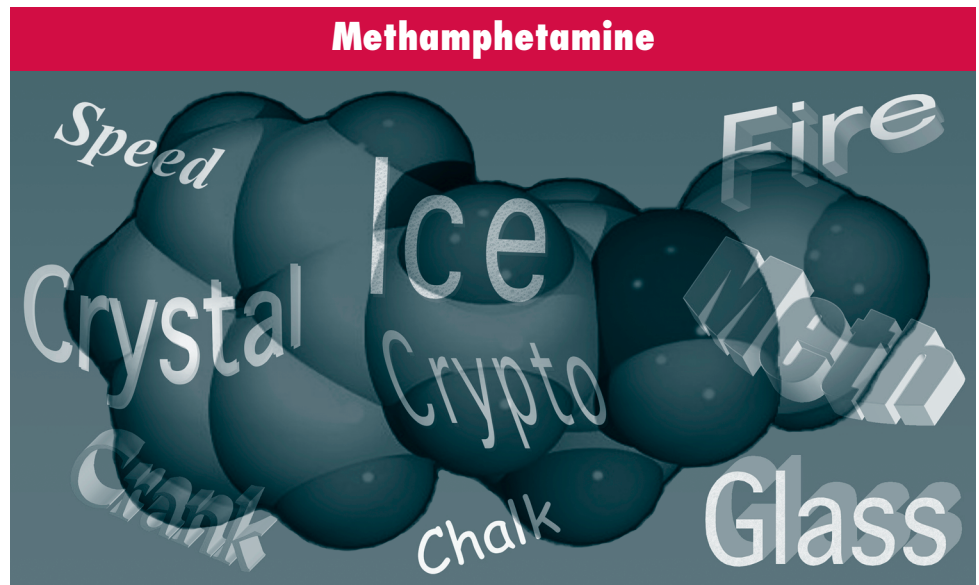
### *Abuse and Addiction*

#### What is methamphetamine?

**M**ethamphetamine is a highly addictive stimulant that affects the central nervous system. Although most of the methamphetamine used in this country comes from foreign or domestic superlabs, the drug is also easily made in small clandestine laboratories, with relatively inexpensive over-the-counter ingredients. These factors combine to make meth-

amphetamine a drug with high potential for widespread abuse.

Methamphetamine is commonly known as “speed,” “meth,” and “chalk.” In its smoked form, it is often referred to as “ice,” “crystal,” “crank,” and “glass.” It is a white, odorless, bitter-tasting crystalline powder that easily dissolves in water or alcohol. The drug was developed early last century from its parent drug,

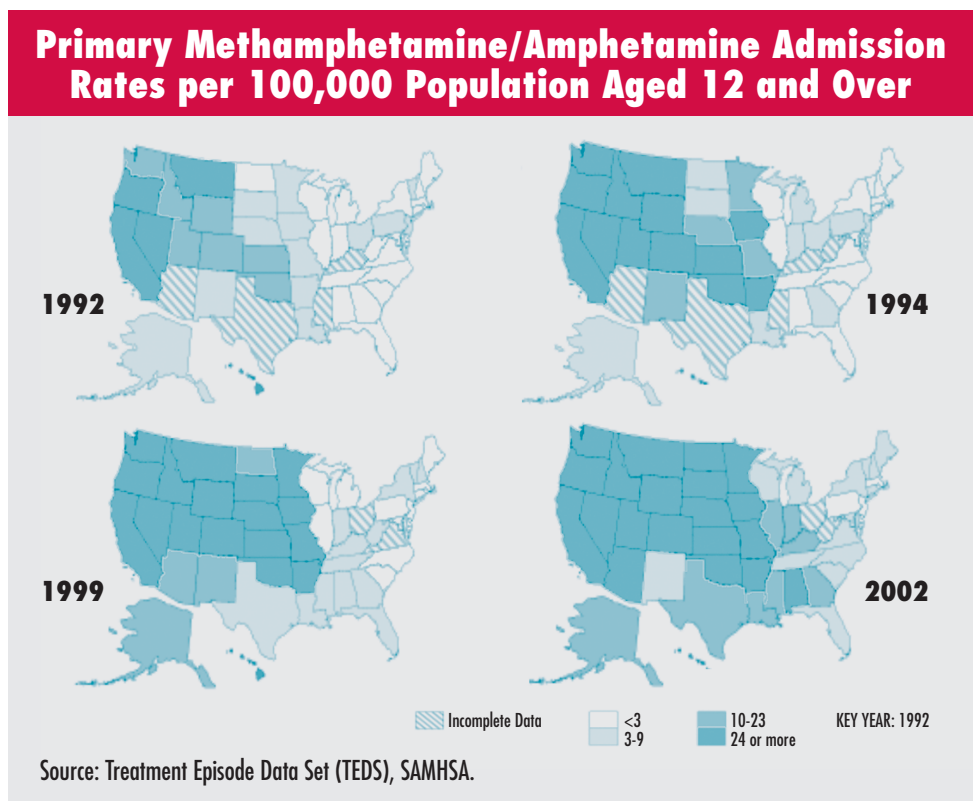


amphetamine, and was used originally in nasal decongestants and bronchial inhalers. Like amphetamine, methamphetamine causes increased activity and talkativeness, decreased appetite, and a general sense of well-being. However, methamphetamine differs from amphetamine in that at comparable doses, much higher levels of methamphetamine get into the brain, making it a more potent stimulant drug. It also has longer lasting and more harmful effects on the central nervous system.

Methamphetamine is a Schedule II stimulant, which means it has a high potential for abuse and is available only through a prescription. It is indicated for the treatment of narcolepsy (a sleep disorder) and attention deficit hyperactivity disorder; but these medical uses are limited, and the doses are much lower than those typically abused.

## What is the scope of methamphetamine abuse in the United States?

**N**IDA's Community Epidemiology Work Group (CEWG), an early warning network of researchers that provides information about the nature and patterns of drug abuse in 21 major areas of the



U.S., reported in January 2006 that methamphetamine continues to be a problem in the West, with indicators persisting at high levels in Honolulu, San Diego, Seattle, San Francisco, and Los Angeles; and that it continues to spread to other areas of the country, including both rural and urban sections of the South and Midwest. In fact, methamphetamine was reported to be the fastest growing problem in metropolitan Atlanta.

According to the 2005 National Survey on Drug Use and Health (NSDUH), an estimated 10.4 million people age 12 or older (4.3 percent of the population) have tried methamphetamine at some time in their lives. Approximately 1.3 million reported past-year

methamphetamine use, and 512,000 reported current (past-month) use. Moreover, the 2005 Monitoring the Future (MTF) survey of student drug use and attitudes reported 4.5 percent of high school seniors had used methamphetamine within their lifetimes, while 8th-graders and 10th-graders reported lifetime use at 3.1 and 4.1 percent, respectively. However, neither of these surveys has documented an overall increase in the abuse of methamphetamine over the past few years. In fact, both surveys showed recent declines in methamphetamine abuse among the Nation's youth.

In contrast, evidence from emergency departments and treatment programs attest to

the growing impact of methamphetamine abuse in the country. The Drug Abuse Warning Network (DAWN), which collects information on drug-related episodes from hospital emergency departments (EDs) throughout the Nation, has reported a greater than 50 percent increase in the number of ED visits related to methamphetamine abuse between 1995 and 2002, reaching approximately 73,000 ED visits, or 4 percent of all drug-related visits in 2004.

Treatment admissions for methamphetamine abuse have also increased substantially. In 1992, there were approximately 21,000 treatment admissions in which methamphetamine/amphetamine was identified as the primary drug of abuse, representing more than 1 percent of all treatment admissions during the year. By 2004, the number of methamphetamine treatment admissions increased to greater than 150,000, representing 8 percent of all admissions.

Moreover, this increased involvement of methamphetamine in drug treatment admissions has also been spreading across the country. In 1992, only 5 states reported high rates of treatment admissions (i.e., >24 per 100,000 population) for primary methamphetamine/amphetamine problems; by 2002, this number increased to 21, more than a third of the states.

## How is methamphetamine abused?

**M**ethamphetamine comes in many forms and can be smoked, snorted, injected, or orally ingested. The preferred method of methamphetamine abuse varies by geographical region and has changed over time. Smoking methamphetamine, which leads to very fast uptake of the drug in the brain, has become more common in recent years, amplifying methamphetamine’s addiction potential and adverse health consequences.

The drug also alters mood in different ways, depending on how it is taken. Immediately after smoking the drug or injecting it intravenously, the user experiences an intense rush or “flash” that lasts only a few minutes and is described as extremely pleasurable. Snorting or oral ingestion produces euphoria—a high but not an

intense rush. Snorting produces effects within 3 to 5 minutes, and oral ingestion produces effects within 15 to 20 minutes.

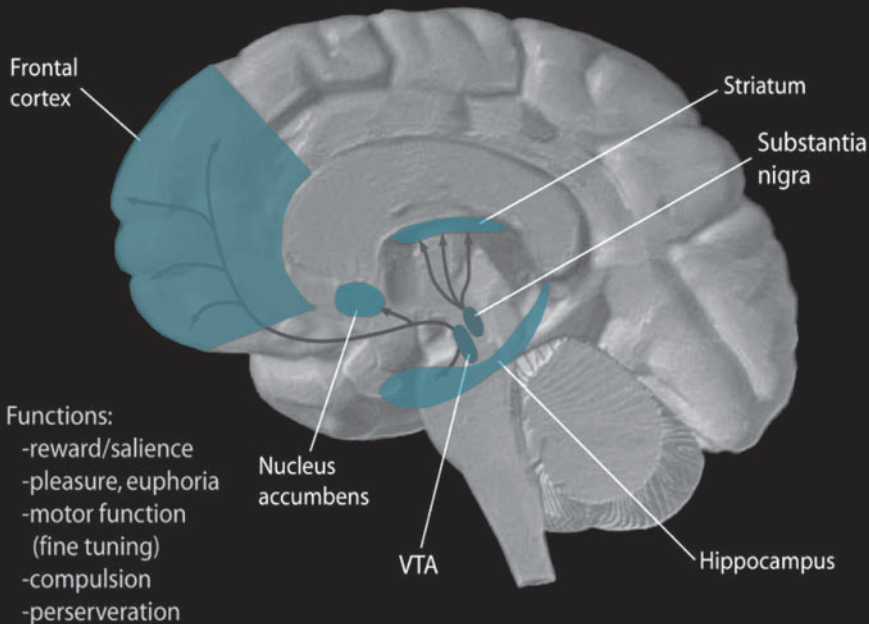
As with similar stimulants, methamphetamine most often is used in a “binge and crash” pattern. Because the pleasurable effects of methamphetamine disappear even before the drug concentration in the blood falls significantly—users try to maintain the high by taking more of the drug. In some cases, abusers indulge in a form of binging known as a “run,” foregoing food and sleep while continuing abuse for up to several days.

## How is methamphetamine different from other stimulants, such as cocaine?

**M**ethamphetamine is structurally similar to amphetamine and the neurotransmitter dopamine, but

Methamphetamine	vs.	Cocaine
Stimulant	—	Stimulant and local anesthetic
Man-made	—	Plant-derived
Smoking produces a long-lasting high	—	Smoking produces a brief high
50% of the drug is removed from the body in 12 hours	—	50% of the drug is removed from the body in 1 hour
Increases dopamine release and blocks dopamine re-uptake	—	Blocks dopamine re-uptake
Limited medical use	—	Limited use as a local anesthetic in some surgical procedures

## Dopamine Pathways



In the brain, dopamine plays an important role in the regulation of reward and movement. As part of the reward pathway, dopamine is manufactured in nerve cell bodies located within the ventral tegmental area (VTA) and is released in the nucleus accumbens and the prefrontal cortex. Its motor functions are linked to a separate pathway, with cell bodies in the substantia nigra that manufacture and release dopamine into the striatum.

it is quite different from cocaine. Although these stimulants have similar behavioral and physiological effects, there are some major differences in the basic mechanisms of how they work. In contrast to cocaine, which is quickly removed and almost completely metabolized in the body, methamphetamine has a much longer duration of action and a larger percentage of the drug remains unchanged in the body. This results in methamphetamine being present in the brain longer, which ultimately leads to prolonged stimulant effects. And

although both methamphetamine and cocaine increase levels of the brain chemical dopamine, animal studies reveal much higher levels of dopamine following administration of methamphetamine due to the different mechanisms of action within nerve cells in response to these drugs. Cocaine prolongs dopamine actions in the brain by blocking dopamine re-uptake. While at low doses, methamphetamine blocks dopamine re-uptake, methamphetamine also increases the release of dopamine, leading to much

higher concentrations in the synapse, which can be toxic to nerve terminals.

## What are the immediate (short-term) effects of methamphetamine abuse?

**A**s a powerful stimulant, methamphetamine, even in small doses, can increase wakefulness and physical activity and decrease appetite. Methamphetamine can also cause a variety of cardiovascular problems, including rapid heart rate, irregular heartbeat, and increased blood pressure. Hyperthermia (elevated body temperature) and convulsions may occur with methamphetamine overdose, and if not treated immediately, can result in death.

Most of the pleasurable effects of methamphetamine are believed to result from the release of very high levels of the neurotransmitter dopamine. Dopamine is involved in motivation, the experience of pleasure, and motor function, and is a common mechanism of action for most drugs of abuse. The elevated release of dopamine produced by methamphetamine is also thought to contribute to the drug's deleterious effects on nerve terminals in the brain.

## What are the long-term effects of methamphetamine abuse?

**L**ong-term methamphetamine abuse has many negative consequences, including addiction. Addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use, accompanied by functional and molecular changes in the brain. In addition to being addicted to methamphetamine, chronic abusers exhibit symptoms that can include anxiety, confusion, insomnia, mood disturbances, and violent behavior. They also can display a number of psychotic features, including paranoia, visual and auditory hallucinations, and delusions (for example, the sensation of

insects creeping under the skin). Psychotic symptoms can sometimes last for months or years after methamphetamine abuse has ceased, and stress has been shown to precipitate spontaneous recurrence of methamphetamine psychosis in formerly psychotic methamphetamine abusers.

With chronic abuse, tolerance to methamphetamine's pleasurable effects can develop. In an effort to intensify the desired effects, abusers may take higher doses of the drug, take it more frequently, or change their method of drug intake. Withdrawal from methamphetamine occurs when a chronic abuser stops taking the drug; symptoms of withdrawal include depression, anxiety, fatigue, and an intense craving for the drug.

Chronic methamphetamine abuse also significantly changes the brain. Specifically, brain

imaging studies have demonstrated alterations in the activity of the dopamine system that are associated with reduced motor speed and impaired verbal learning. Recent studies in chronic methamphetamine

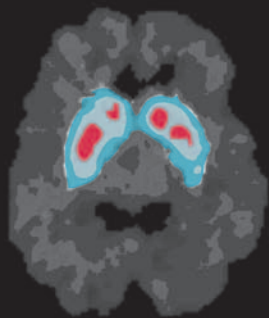
### Short-Term Effects May Include:

- Increased attention and decreased fatigue
- Increased activity and wakefulness
- Decreased appetite
- Euphoria and rush
- Increased respiration
- Rapid/irregular heartbeat
- Hyperthermia

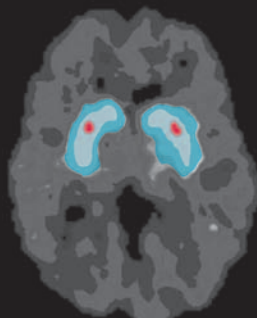
### Long-Term Effects May Include:

- Addiction
- Psychosis, including:
  - paranoia
  - hallucinations
  - repetitive motor activity
- Changes in brain structure and function
- Memory loss
- Aggressive or violent behavior
- Mood disturbances
- Severe dental problems
- Weight loss

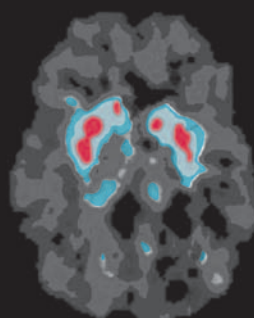
### Recovery of Brain Dopamine Transporters in Chronic Methamphetamine (METH) Abusers



Normal Control



METH Abuser  
(1 month abstinence)



METH Abuser  
(24 month abstinence)

Source: Volkow ND et al., *Journal of Neuroscience* 21:9414–9418, 2001.

abusers have also revealed severe structural and functional changes in areas of the brain associated with emotion and memory, which may account for many of the emotional and cognitive problems observed in chronic methamphetamine abusers.

Fortunately, some of the effects of chronic methamphetamine abuse appear to be, at least partially, reversible. A recent neuroimaging study showed recovery in some brain regions following prolonged abstinence (2 years, but not 6 months). This was associated with improved performance on motor and verbal memory tests. However, function in other brain regions did not display recovery even after 2 years of abstinence, indicating that some methamphetamine-induced changes are very long-lasting. Moreover, the increased risk of stroke from the abuse of methamphetamine can lead to irreversible damage to the brain.

## What are the risks of methamphetamine abuse during pregnancy?

**P**renatal exposure to methamphetamine may also be a problem in the United States. Although according

to the NSDUH, less than 1 percent of pregnant women aged 15–44 had used methamphetamine in the past year, any use among this population is of concern. Unfortunately, our knowledge of the effects of methamphetamine during pregnancy is limited. The few human studies that exist have shown increased rates of premature delivery, placental abruption, fetal growth retardation, and heart and brain abnormalities. However, these studies are difficult to interpret due to methodological issues, such as small sample size and maternal use of other drugs. Ongoing research is continuing to study developmental outcomes such as cognition, social relationships, motor skills, and medical status of children exposed to methamphetamine before birth.

## Are methamphetamine abusers at risk for contracting HIV/AIDS and hepatitis B and C?

**I**ncreased HIV and hepatitis B and C transmission are consequences of increased methamphetamine abuse, not only in individuals who inject the drug, but also in noninjecting methamphetamine abusers. Among injection drug users,

infection with HIV and other infectious diseases is spread primarily through the re-use of contaminated syringes, needles, or other paraphernalia by more than one person. However, regardless of how it is taken, the intoxicating effects of methamphetamine can alter judgment and inhibition and lead people to engage in unsafe behaviors.

Methamphetamine has become associated with a culture of risky sexual behavior, both among men who have sex with men (MSM) and heterosexual populations. This link may be due to the fact that methamphetamine and related psychomotor stimulants can increase libido. Paradoxically, long-term methamphetamine abuse may be associated with decreased sexual functioning, at least in men. The combination of injection and sexual risk-taking may result in HIV becoming a greater problem among methamphetamine abusers than among opiate and other drug abusers, something that already seems to be occurring, according to some epidemiologic reports. For example, while the link between HIV infection and methamphetamine abuse has not yet been established for heterosexuals, data show an association between methamphetamine abuse and the spread of HIV among MSM.

Methamphetamine abuse may also worsen the progression of

HIV and its consequences. In animal studies, methamphetamine increased viral replication; in human methamphetamine abusers, HIV caused greater neuronal injury and cognitive impairment compared with nondrug abusers.

NIDA-funded research has found that, through drug abuse treatment, prevention, and community-based outreach programs, drug abusers can change their HIV risk behaviors. Drug abuse can be eliminated and drug-related risk behaviors, such as needle-sharing and unsafe sexual practices, can be reduced significantly, thus decreasing the risk of exposure to HIV and other infectious diseases. Therefore, drug abuse treatment *is* HIV prevention.

## What treatments are effective for methamphetamine abusers?

**A**t this time, the most effective treatments for methamphetamine addiction are behavioral therapies such as cognitive behavioral and contingency management interventions. For example, the Matrix Model, a comprehensive behavioral treatment approach that combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement

for nondrug-related activities, has been shown to be effective in reducing methamphetamine abuse. Contingency management interventions, which provide tangible incentives in exchange for engaging in treatment and maintaining abstinence, have also been shown to be effective.

There are currently no specific medications that counteract the effects of methamphetamine or that prolong abstinence from and reduce the abuse of methamphetamine by an individual addicted to the drug. However, there are a number of medications that are FDA-approved for other illnesses that might also be useful in treating methamphetamine addiction. Recent study findings reveal that bupropion, the anti-depressant marketed as Wellbutrin, reduced the methamphetamine-induced “high” as well as drug cravings elicited by drug-related cues. This medication and others are currently in clinical trials, while new compounds are being developed and studied in preclinical models.

## Where can I get further scientific information about methamphetamine abuse?

**T**o learn more about methamphetamine and other drugs of abuse, contact the National Clearing-

house for Alcohol and Drug Information (NCADI) at 800-729-6686. Information specialists are available to help you locate information and resources.

Fact sheets, including *InfoFacts*, on the health effects of methamphetamine, other drugs of abuse, and other drug abuse topics are available on the NIDA Web site ([www.drugabuse.gov](http://www.drugabuse.gov)), and can be ordered free of charge in English and Spanish from NCADI at [www.health.org](http://www.health.org).

### Access information on the Internet

- What’s new on the NIDA Web site
- Information on drugs of abuse
- Publications and communications (including *NIDA Notes*)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

#### NIDA Web Sites

[www.drugabuse.gov](http://www.drugabuse.gov)  
[www.steroidabuse.gov](http://www.steroidabuse.gov)  
[www.clubdrugs.gov](http://www.clubdrugs.gov)  
[www.hiv.drugabuse.gov](http://www.hiv.drugabuse.gov)  
[www.inhalant.drugabuse.gov](http://www.inhalant.drugabuse.gov)

#### NCADI

Web Site: [www.health.org](http://www.health.org)  
 Phone No.: 800-729-6686

## Glossary

**Addiction:** A chronic, relapsing disease, characterized by compulsive drug seeking and drug use and by neurochemical and molecular changes in the brain.

**Attention deficit hyperactivity disorder:** A disorder that often presents in early childhood, characterized by inattention, hyperactivity, and impulsivity.

**Central nervous system (CNS):** The brain and spinal cord.

**Craving:** A powerful, often uncontrollable desire for drugs.

**Dopamine:** A neurotransmitter present in regions of the brain that regulate movement, emotion, motivation, and feelings of pleasure.

**Narcolepsy:** A disorder characterized by uncontrollable attacks of deep sleep.

**Psychomotor stimulants (psychostimulants):** Drugs that increase or enhance the activity of monoamines (such as dopamine and norepinephrine) in the brain. Psychostimulants increase arousal and activity, as well as heart rate, blood pressure, and respiration.

**Psychosis:** A mental disorder characterized by symptoms such as delusions or hallucinations and disordered thinking.

**Rush:** A surge of euphoric pleasure that rapidly follows administration of a drug.

**Tolerance:** A condition in which higher doses of a drug are required to produce the same effect as experienced initially.

**Toxic:** Damage to an organ or group of organs.

**Withdrawal:** A variety of symptoms that occur after chronic abuse of an addictive drug is reduced or stopped.

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ON DRUG ABUSE

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What are the medical consequences of tobacco use? See page 4.

## Research Report Series

### from the director:

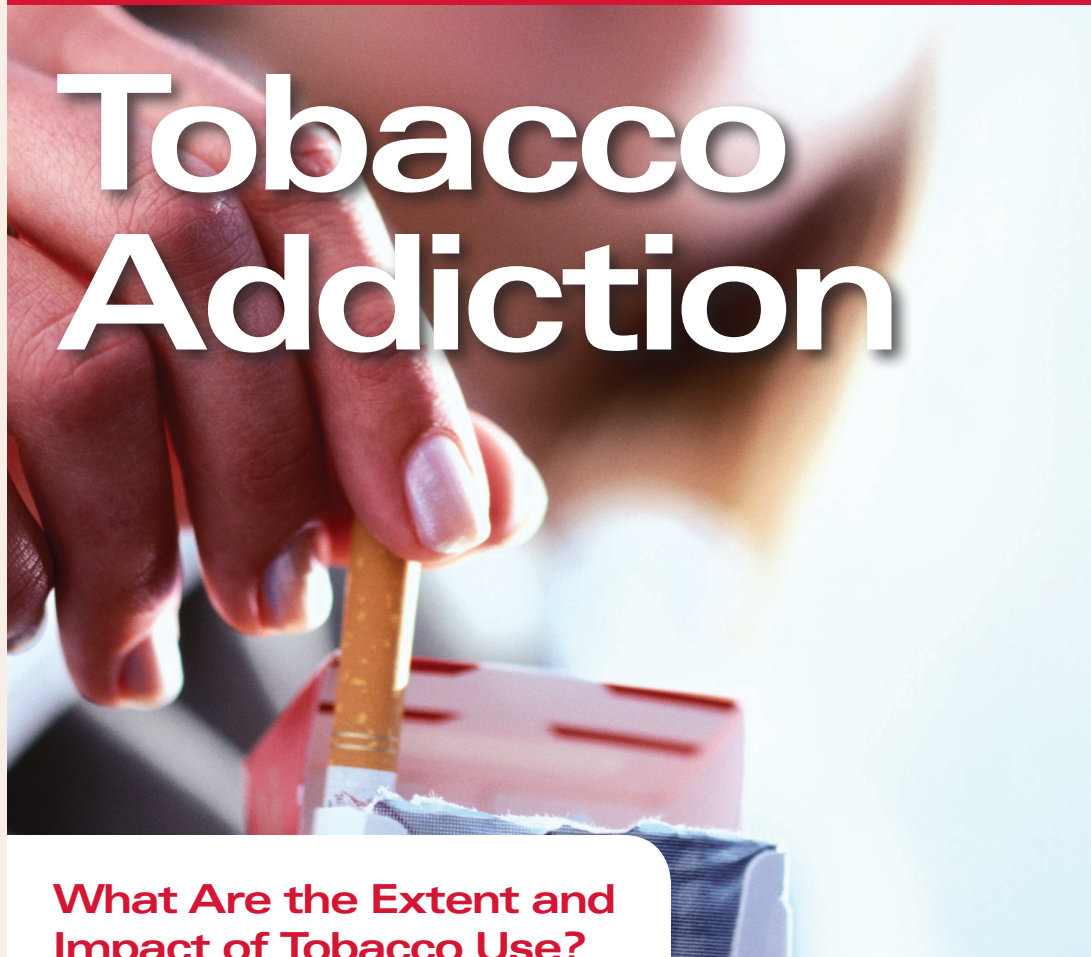
Tobacco use kills approximately 440,000 Americans each year, with one in every five U.S. deaths the result of smoking. Smoking harms nearly every organ in the body, causes many diseases, and compromises smokers' health in general. Nicotine, a component of tobacco, is the primary reason that tobacco is addictive, although cigarette smoke contains many other dangerous chemicals, including tar, carbon monoxide, acetaldehyde, nitrosamines, and more.

An improved overall understanding of addiction and of nicotine as an addictive drug has been instrumental in developing medications and behavioral treatments for tobacco addiction. For example, the nicotine patch and gum, now readily available at drugstores and supermarkets nationwide, have proven effective for smoking cessation when combined with behavioral therapy.

Advanced neuroimaging technologies make it possible for researchers to observe changes in brain function that result from smoking tobacco. Researchers are now also identifying genes that predispose people to tobacco addiction and predict their response to smoking cessation treatments. These findings—and many other recent research accomplishments—present unique opportunities to discover, develop, and disseminate new treatments for tobacco addiction, as well as scientifically based prevention programs to help curtail the public health burden that tobacco use represents.

We hope this *Research Report* will help readers understand the harmful effects of tobacco use and identify best practices for the prevention and treatment of tobacco addiction.

Nora D. Volkow, M.D.  
Director  
National Institute on Drug Abuse



# Tobacco Addiction

## What Are the Extent and Impact of Tobacco Use?

**A**ccording to the 2007 National Survey on Drug Use and Health, an estimated 70.9 million Americans aged 12 or older reported current use of tobacco—60.1 million (24.2 percent of the population) were current cigarette smokers, 13.3 million (5.4 percent) smoked cigars, 8.1 million (3.2 percent) used smokeless tobacco, and 2 million (0.8 percent) smoked pipes, confirming that tobacco is one of the most widely abused substances in the United States. Although the numbers of people who smoke are still unacceptably high, according

*continued inside*

to the Centers for Disease Control and Prevention there has been a decline of almost 50 percent since 1965.

NIDA's 2008 Monitoring the Future survey of 8th-, 10th-, and 12th-graders, which is used to track drug use patterns and attitudes, has also shown a striking decrease in smoking trends among the Nation's youth. The latest results indicate that about 7 percent of 8th-graders, 12 percent of 10th-graders, and 20 percent of 12th-graders had used cigarettes in the 30 days prior to the survey—the lowest levels in the history of the survey.

The declining prevalence of cigarette smoking among the general U.S. population, how-

ever, is not reflected in patients with mental illnesses. The rate of smoking in patients suffering from post-traumatic stress disorder, bipolar disorder, major depression, and other mental illness is two- to fourfold higher than in the general population; and among people with schizophrenia, smoking rates as high as 90 percent have been reported.

Tobacco use is the leading preventable cause of death in the United States. The impact of tobacco use in terms of morbidity and mortality to society is staggering.

Economically, more than \$96 billion of total U.S. health care costs each year are attributable directly to smoking.

However, this is well below the total cost to society because it does not include burn care from smoking-related fires, perinatal care for low-birthweight infants of mothers who smoke, and medical care costs associated with disease caused by secondhand smoke. In addition to health care costs, the costs of lost productivity due to smoking effects are estimated at \$97 billion per year, bringing a conservative estimate of the economic burden of smoking to more than \$193 billion per year.

### How Does Tobacco Deliver Its Effects?

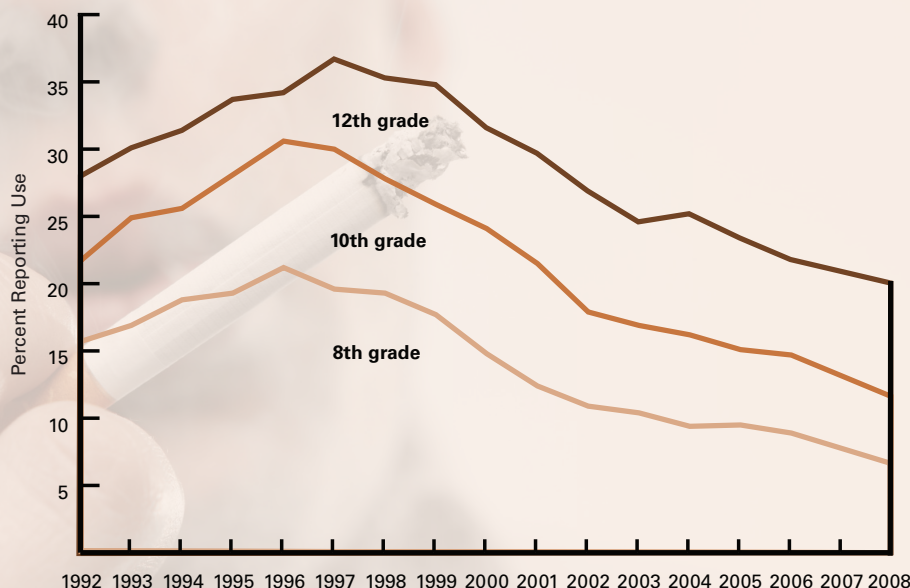
There are more than 4,000 chemicals found in the smoke of tobacco products. Of these, nicotine, first identified in the early 1800s, is the primary reinforcing component of tobacco.

Cigarette smoking is the most popular method of using tobacco; however, there has also been a recent increase in the use of smokeless tobacco products, such as snuff and chewing tobacco. These smokeless products also contain nicotine, as well as many toxic chemicals.

The cigarette is a very efficient and highly engineered drug delivery system. By inhaling tobacco smoke, the average smoker takes in 1–2 mg of nicotine per cigarette. When tobacco is smoked, nicotine rapidly reaches peak levels in the bloodstream and enters the brain. A typical smoker will take 10 puffs on a cigarette over a period of 5 minutes that

### Trends in Prevalence of Cigarette Use for 8th-, 10th-, and 12th-Graders

Percentage of Students Using Cigarettes Over a 30-Day Period, 1992–2008



Source: University of Michigan, 2008 Monitoring the Future Survey.

the cigarette is lit. Thus, a person who smokes about 1½ packs (30 cigarettes) daily gets 300 “hits” of nicotine to the brain each day. In those who typically do not inhale the smoke—such as cigar and pipe smokers and smokeless tobacco users—nicotine is absorbed through the mucosal membranes and reaches peak blood levels and the brain more slowly.

Immediately after exposure to nicotine, there is a “kick” caused in part by the drug’s stimulation of the adrenal glands and resulting discharge of epinephrine (adrenaline). The rush of adrenaline stimulates the body and causes an increase in blood pressure, respiration, and heart rate.

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## Is Nicotine Addictive?

Yes. Most smokers use tobacco regularly because they are addicted to nicotine. Addiction is characterized by compulsive drug seeking and abuse, even in the face of negative health consequences. It is well documented that most smokers identify tobacco use as harmful and express a desire to reduce or stop using it, and nearly 35 million of them want to quit each year. Unfortunately, more than 85 percent of those who try to quit on their own relapse, most within a week.

Research has shown how nicotine acts on the brain to produce a number of effects. Of primary importance to its addictive nature are findings that nicotine activates reward pathways—the brain circuitry that regulates feelings of pleasure. A key brain chemical involved in mediating the desire to consume drugs is the neurotransmitter dopamine, and research

has shown that nicotine increases levels of dopamine in the reward circuits. This reaction is similar to that seen with other drugs of abuse and is thought to underlie the pleasurable sensations experienced by many smokers. For many tobacco users, long-term brain changes induced by continued nicotine exposure result in addiction.

Nicotine’s pharmacokinetic properties also enhance its abuse potential. Cigarette smoking produces a rapid distribution of nicotine to the brain, with drug levels peaking within 10 seconds of inhalation. However, the acute effects of nicotine dissipate quickly, as do the associated feelings of reward, which causes the smoker to continue dosing to maintain the drug’s pleasurable effects and prevent withdrawal.

Nicotine withdrawal symptoms include irritability, craving, depression, anxiety, cognitive and attention deficits, sleep disturbances, and increased appetite. These symptoms may begin within a few hours after the last cigarette, quickly driving people back to tobacco use. Symptoms peak within the first few days of smoking cessation and usually subside within a few weeks. For some people, however, symptoms may persist for months.

Although withdrawal is related to the pharmacological effects of nicotine, many behavioral factors can also affect the severity of withdrawal symptoms. For some people, the feel, smell, and sight of a cigarette and the ritual of obtaining, handling, lighting, and smoking the cigarette are all associated with the pleasurable effects of smoking and can make withdrawal or craving worse. Nicotine replacement therapies such as gum, patches, and inhalers may help alleviate the pharma-



*Tobacco plants*

***Most smokers identify tobacco use as harmful and express a desire to reduce or stop using it, and nearly 35 million want to quit each year.***

cological aspects of withdrawal; however, cravings often persist. Behavioral therapies can help smokers identify environmental triggers of craving so they can employ strategies to prevent or circumvent these symptoms and urges.

**Nicotine replacement therapies such as gum, patches, and inhalers may help alleviate the pharmacological aspects of withdrawal.**

## Are There Other Chemicals That May Contribute to Tobacco Addiction?

Yes, research is showing that nicotine may not be the only ingredient in tobacco that affects its addictive potential. Using advanced neuroimaging technology, scientists can see the dramatic effect of cigarette smoking on the brain and are finding a marked decrease in the levels of monoamine oxidase (MAO), an important enzyme that is responsible for the breakdown of dopamine. This change is likely caused by some ingredient in tobacco smoke other than nicotine, because we know that nicotine itself does not dramatically alter MAO levels. The decrease in two forms of MAO (A and B) results in higher dopamine levels and may be another reason that smokers continue to smoke—to sustain the high dopamine levels that lead to the desire for repeated drug use.

Animal studies by NIDA-funded researchers have shown that acetaldehyde, another chemical found in tobacco smoke, dramatically increases the reinforcing properties of nicotine and may also contribute to tobacco addiction. The investigators further report that this effect is age-related: adolescent

animals display far more sensitivity to this reinforcing effect, which suggests that the brains of adolescents may be more vulnerable to tobacco addiction.

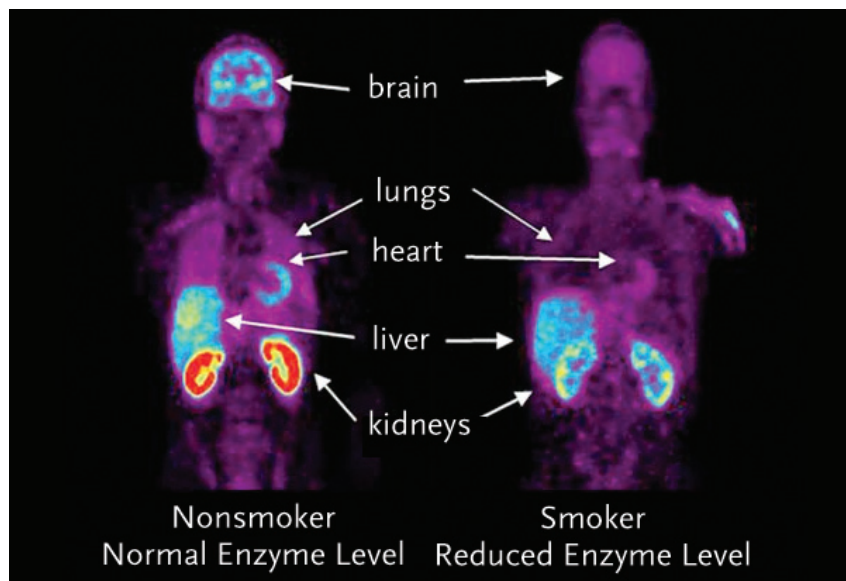
## What Are the Medical Consequences of Tobacco Use?

Cigarette smoking kills an estimated 440,000 U.S. citizens each year—more than alcohol, illegal drug use, homicide, suicide, car accidents, and AIDS combined. Between 1964 and 2004, more than 12 million Americans died prematurely from smoking, and another 25 million U.S. smokers alive today will most likely die of a smoking-related illness.

Cigarette smoking harms nearly every organ in the body. It has been conclusively linked to cataracts and pneumonia, and accounts for about one-third of all cancer deaths. The

overall rates of death from cancer are twice as high among smokers as nonsmokers, with heavy smokers having rates that are four times greater than those of nonsmokers. Foremost among the cancers caused by tobacco use is lung cancer—cigarette smoking has been linked to about 90 percent of all cases of lung cancer, the number one cancer killer of both men and women. Smoking is also associated with cancers of the mouth, pharynx, larynx, esophagus, stomach, pancreas, cervix, kidney, bladder, and acute myeloid leukemia.

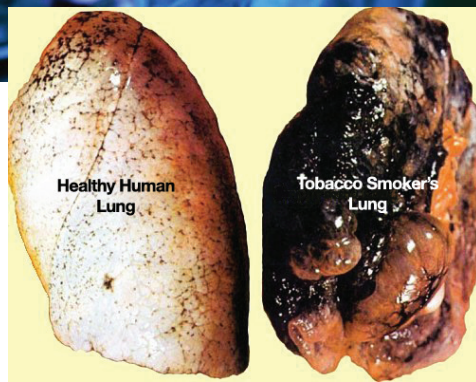
In addition to cancer, smoking causes lung diseases such as chronic bronchitis and emphysema, and it has been found to exacerbate asthma symptoms in adults and children. About 90 percent of all deaths from chronic obstructive pulmonary diseases are attributable to cigarette smoking. It has also been well documented that smoking substantially increases the risk of heart disease, including stroke, heart attack, vascular



*Using advanced neuroimaging technology, scientists can see the dramatic effect of cigarette smoking on the brain and body and are finding a marked decrease in the levels of monoamine oxidase (MAO B), an important enzyme that is responsible for the breakdown of dopamine. (Source: Fowler et al., 2003)*



*Sticky, brown tar coats the lungs of tobacco smokers. Along with thousands of other damaging chemicals, tar can lead to lung cancer and acute respiratory diseases.*



disease, and aneurysm. Smoking causes coronary heart disease, the leading cause of death in the United States: cigarette smokers are 2–4 times more likely to develop coronary heart disease than nonsmokers.

Exposure to high doses of nicotine, such as those found in some insecticide sprays, can be extremely toxic as well, causing vomiting, tremors, convulsions, and death. In fact, one drop of pure nicotine can kill a person. Nicotine poisoning has been reported from accidental ingestion of insecticides by adults and ingestion of tobacco products by children and pets. Death usually results in a few minutes from respiratory failure caused by paralysis.

Although we often think of medical consequences that result from direct use of tobacco products, passive or secondary smoke also increases the risk for many diseases. Environmental tobacco smoke is a major source of indoor air contaminants; secondhand smoke is estimated to cause approximately 3,000 lung cancer deaths per year among nonsmokers and contributes to more than 35,000 deaths related to cardiovascular disease. Exposure to tobacco smoke in the home is also a risk factor for new cases and increased severity of childhood asthma. Additionally, dropped cigarettes are the leading cause of residential fire fatalities, leading to more than 1,000 deaths each year.

## Are There Safe Tobacco Products?

The adverse health effects of tobacco use are well known, yet many people do not want to quit or have difficulty quitting. As a result, there has been a recent surge in the development of tobacco products that claim to reduce exposure to harmful tobacco constituents or to have fewer health risks than conventional products. These “potentially reduced exposure products” (PREPs), which include cigarettes and smokeless tobacco (e.g., snuff, tobacco lozenges), have not yet been evaluated sufficiently to determine whether they are indeed associated with reduced risk of disease. Recent studies indicate that the levels of carcinogens in these PREPs range from relatively low to comparable to conventional tobacco products. These studies conclude that medicinal nicotine (found in the nicotine patch and gum) is a safer alternative than these modified tobacco products.

## Tobacco Use and Comorbidity

There is clear evidence of high rates of psychiatric comorbidity, including other substance abuse, among adolescents and adults who smoke. For example, it has been estimated that individuals with psychiatric disorders purchase approximately 44 percent of all cigarettes sold in the United States, which undoubtedly contributes to the disproportionate rates of morbidity and mortality in these populations. In addition, studies have shown that as many as 80 percent of alcoholics smoke regularly, and that a majority of them will die of smoking-related, rather than alcohol-related, disease.

In young smokers, the behavior appears to be strongly associated with increased risk for a variety of mental disorders. In some cases—such as with conduct disorders and attention-deficit hyperactivity disorder—these disorders may precede the onset of smoking, while in others—such as with substance abuse—the disorders may emerge later in life. Whether daily smoking among boys and girls is the result or the cause of a manifest psychiatric condition, it is troubling that so very few adolescents have their

nicotine dependence diagnosed or properly treated. Preventing the early onset of smoking and treating its young victims are critical primary-care priorities, the fulfillment of which could have a dramatic impact on our ability to prevent or better address a wide range of mental disorders throughout life.

Among adults, the rate of major depressive episodes is highest in nicotine-dependent individuals, lower in nondependent current smokers, and lowest in those who quit or never started smoking. Furthermore, there is evidence showing that, for those who have had more than one episode, smoking cessation may increase the likelihood of a new major depressive episode. Adult tobacco use also increases risk for the later development of anxiety disorders, which may be associated with an increased severity of withdrawal symptoms during smoking cessation therapy. But the most extensive comorbidity overlap is likely the one that exists between smoking and schizophrenia, since, in clinical samples, the rate of smoking in patients with schizophrenia has ranged as high as 90 percent.

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### Smoking and Pregnancy— What Are the Risks?

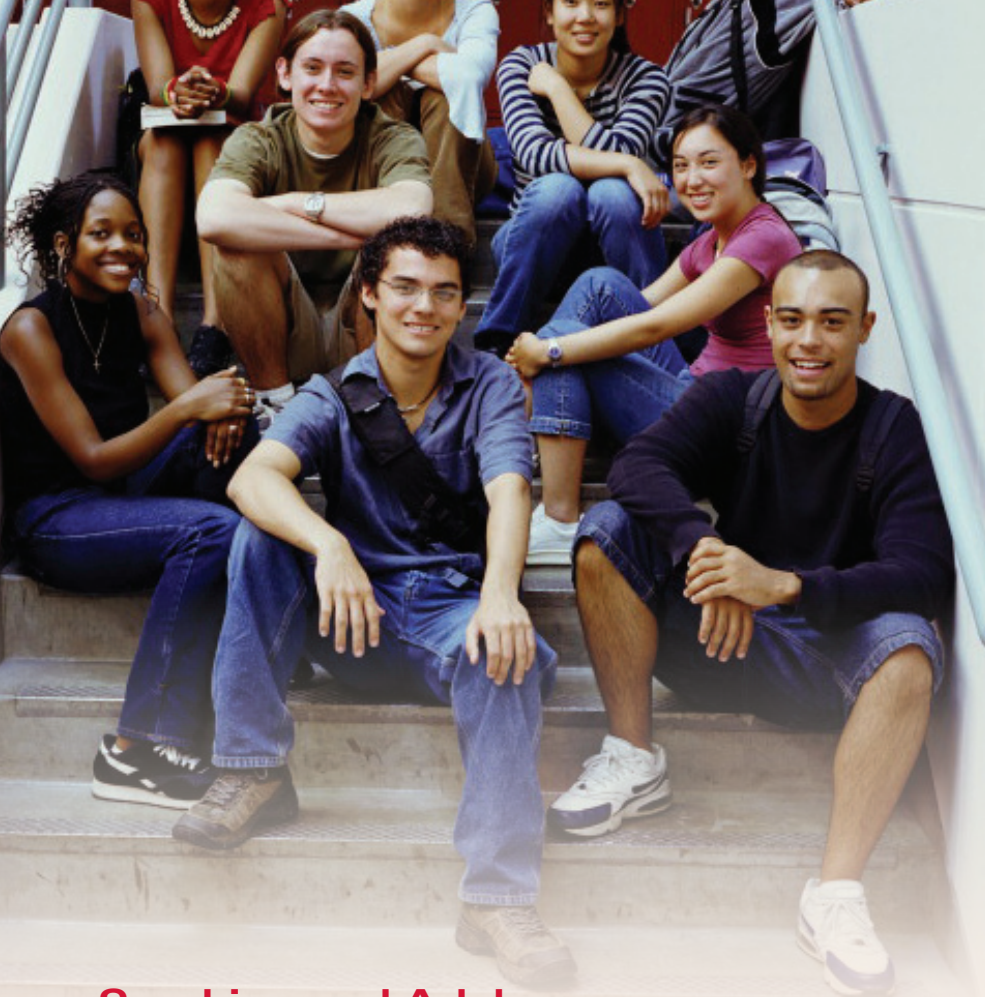
In the United States, it is estimated that about 16 percent of pregnant women smoke during their pregnancies. Carbon monoxide and nicotine from tobacco smoke may interfere with the oxygen supply to the fetus. Nicotine also readily crosses the placenta, and concentrations in the fetus can be as much as 15 percent higher than maternal levels. Nicotine concentrates in fetal blood, amniotic fluid, and breast milk. Combined, these factors can have severe consequences for the fetuses and infants of smoking mothers. Smoking

during pregnancy caused an estimated 910 infant deaths annually from 1997 through 2001, and neonatal care costs related to smoking are estimated to be more than \$350 million per year.

The adverse effects of smoking during pregnancy can include fetal growth retardation and decreased birthweight. The decreased birthweights seen in infants of mothers who smoke reflect a dose-dependent relationship—the more the woman smokes during pregnancy, the greater the reduction of infant birthweight. These newborns also display signs of stress and drug withdrawal consistent with what has been reported in infants exposed to other drugs. In some cases, smoking during pregnancy may be associated with spontaneous abortions and sudden infant death syndrome



(SIDS), as well as learning and behavioral problems and an increased risk of obesity in children. In addition, smoking more than one pack a day during pregnancy nearly doubles the risk that the affected child will become addicted to tobacco if that child starts smoking.



## Smoking and Adolescence

In 2007, more than 3 million American adolescents (aged 12–17) reported using a tobacco product in the month prior to the survey. In that same year it was found that nearly 60 percent of new smokers were under the age of 18 when they first smoked a cigarette. Of smokers under 18, more than 6 million will likely die prematurely from a smoking-related disease.

Tobacco use in teens is not only the result of psychosocial influences, such as peer pressure; recent research suggests that there may be biological reasons for this period of increased vulnerability. There is some evidence that intermittent smoking can result in the development of tobacco addiction in some teens. Animal models of teen smoking provide additional evidence of an increased vulnerability. Adolescent rats are more susceptible to the reinforcing effects of nicotine than adult rats, and take more nicotine when it is available than do adult animals.

Adolescents may also be more sensitive to the reinforcing effects of nicotine in combination with other chemicals found in cigarettes, thus increasing susceptibility to tobacco addiction. As mentioned above, acetaldehyde increases nicotine's addictive properties in adolescent, but not adult, animals. A recent study also suggests that specific genes may increase risk for addiction among people who begin smoking during adolescence. NIDA continues to actively support research aimed at increasing our understanding of why and how adolescents become addicted, and to develop prevention and treatment strategies to meet their specific needs.

## Are There Gender Differences in Tobacco Smoking?

Several avenues of research now indicate that men and women differ in their smoking behaviors. For instance, women smoke fewer cigarettes per day, tend to use cigarettes with lower nicotine content, and do not inhale as deeply as men. However, it is unclear whether this is due to differences in sensitivity to nicotine or other factors that affect women differently, such as social factors or the sensory aspects of smoking.

The number of smokers in the United States declined in the 1970s and 1980s, remained relatively stable throughout the 1990s, and



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declined further through the early 2000s. Because this decline in smoking was greater among men than women, the prevalence of smoking is only slightly higher for men today than it is for women. Several factors appear to be contributing to this narrowing gender gap, including women being less likely than men to quit.

Large-scale smoking cessation trials show that women are less likely to initiate quitting and may be more likely to relapse if they do quit. In cessation programs using nicotine replacement methods, such as the patch or gum, the nicotine does not seem to reduce craving as effectively for women as for men. Other factors that may contribute to women's difficulty with quitting are that withdrawal may be more intense for women or that women are more concerned about weight gain.

Although postcessation weight gain is typically modest (about

5–10 pounds), concerns about this may be an obstacle to treatment success. In fact, NIDA research has found that when women's weight concerns were addressed during cognitive-behavioral therapy, they were more successful at quitting than women who were in a program designed only to attenuate postcessation weight gain. Other NIDA researchers have found that medications used for smoking cessation, such as bupropion and naltrexone, can also attenuate postcessation weight gain and could become an additional strategy for enhancing treatment success.

It is important for treatment professionals to be aware that standard regimens may have to be adjusted to compensate for gender differences in nicotine sensitivity and in other related factors that contribute to continued smoking.

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## **Are There Effective Treatments for Tobacco Addiction?**

Yes, extensive research has shown that treatments for tobacco addiction do work. Although some smokers can quit without help, many individuals need assistance with quitting. This is particularly important because smoking cessation can have immediate health benefits. For example, within 24 hours of quitting, blood pressure and chances of heart attack decrease. Long-term benefits of smoking cessation include decreased risk of stroke, lung and other cancers, and coronary heart disease. A 35-year-old man who quits smoking will, on average, increase his life expectancy by 5 years.

## **Nicotine Replacement Treatments**



Nicotine replacement therapies (NRTs), such as nicotine gum and the transdermal nicotine patch, were the first pharmacological treatments approved by the Food and Drug Administration (FDA) for use in smoking cessation therapy. NRTs are used (in conjunction with behavioral support) to relieve withdrawal symptoms—they produce less severe physiological alterations than tobacco-based systems and generally provide users with lower overall nicotine levels than they receive with tobacco. An added benefit is that these forms of nicotine have little abuse potential since they do not produce the pleasurable effects of tobacco products, nor do they contain the carcinogens and gases associated with tobacco smoke. Behavioral treatments, even beyond what is recommended on packaging labels, have been shown to enhance the effectiveness of NRTs and improve long-term outcomes.

The FDA's approval of nicotine gum in 1984 marked the availability (by prescription) of the first NRT on the U.S. market. In 1996, the FDA approved Nicorette gum for over-the-counter (OTC) sales. Whereas nicotine gum provides some smokers with the desired control over dose and the ability to relieve cravings, others are unable to tolerate the taste and chewing demands. In 1991 and 1992, the FDA approved four transdermal



nicotine patches, two of which became OTC products in 1996. In 1996 a nicotine nasal spray, and in 1998 a nicotine inhaler, also became available by prescription, thus meeting the needs of many additional tobacco users. All the NRT products—gum, patch, spray, and inhaler—appear to be equally effective.

### Additional Medications

Although the primary focus of pharmacological treatments for tobacco addiction has been nicotine replacement, other treatments are also available. For example, the antidepressant bupropion was approved by the FDA in 1997 to help people quit smoking and is marketed as Zyban. Varenicline



tartrate (Chantix) is a medication that recently received FDA approval for smoking cessation. This medication, which acts at the sites in the brain affected by nicotine, may help people quit by easing withdrawal symptoms and blocking the effects of nicotine if people resume smoking.

Several other nonnicotine medications are being investigated for the treatment of tobacco addiction, including other antidepressants and an antihypertensive medication. Scientists are also investigating the potential of a vaccine that targets nicotine for use in relapse prevention. The nicotine vaccine is designed to stimulate the production of antibodies that would block access of

*Twin studies indicate that approximately 40–70 percent of a person’s risk of becoming addicted to nicotine depends on his or her genes.*



nicotine to the brain and prevent nicotine’s reinforcing effects.

### Behavioral Treatments

Behavioral interventions play an integral role in smoking cessation treatment, either in conjunction with medication or alone. A variety of methods can assist smokers with quitting, ranging from self-help materials to individual cognitive-behavioral therapy. These interventions teach individuals to recognize high-risk smoking situations, develop alternative coping strategies, manage stress, improve problemsolving skills, and increase social support. Research has also shown that the more therapy is tailored to a person’s situation, the greater the chances are for success.

Traditionally, behavioral approaches were developed and delivered through formal settings, such as smoking cessation clinics and community and public health settings. Over the past decade, however, researchers have been adapting these approaches for mail, telephone, and Internet formats, which can be more acceptable and accessible to smokers who are trying to quit. In 2004, the U.S. Department of Health and Human Services (HHS) established a national toll-free number, 800-QUIT-NOW (800-784-8669),

to serve as a single access point for smokers seeking information and assistance in quitting. Callers to the number are routed to their State’s smoking cessation quitline or, in States that have not established quitlines, to one maintained by the National Cancer Institute. In addition, a new HHS Web site ([www.smokefree.gov](http://www.smokefree.gov)) offers online advice and downloadable information to make cessation easier.



Quitting smoking can be difficult. People can be helped during the time an intervention is delivered; however, most intervention programs are short-term (1–3 months). Within 6 months, 75–80 percent of people who try to quit smoking relapse. Research has now shown that extending treatment beyond the typical duration of a smoking cessation program can produce quit rates as high as 50 percent at 1 year.

## New Frontiers in Tobacco Research

If so many smokers want to quit, why are few able to do so successfully? To address this question, scientists are increasingly focusing on the powerful role of genetics in addiction. Twin studies indicate that approximately 40–70 percent of a person’s risk of becoming addicted to nicotine depends on his or her genes. Although complex diseases like addiction involve large numbers of genes interacting with a wide variety of environmental factors, the contribution of a particular gene can be substantial:

Genetic variants associated with nicotine metabolism, for example, have been shown to influence how people smoke such that slow metabolizers smoke fewer cigarettes per day and have a higher likelihood of quitting, and that there is greater abstinence among individuals receiving nicotine patch therapy. A recent NIDA-funded study identified a variant in the gene for a nicotinic receptor subunit that doubled the risk for nicotine addiction among smokers. A subsequent study found that this gene variant also increased susceptibility to the severe health consequences of smoking, including lung cancer and peripheral arterial disease. NIDA is currently supporting large-scale genome-wide associ-

ation studies to uncover additional genetic risk factors in order to better understand tobacco addiction and its adverse effects on health.

In addition to predicting an individual’s risk for nicotine addiction, genetic markers can also help predict whether medications (like bupropion) will effectively help a smoker quit. This takes root in the emerging field of pharmacogenomics, which investigates how genes influence a patient’s response to drugs and medications. In the future, genetic screening could help clinicians select treatments, adjust dosages, and avoid or minimize adverse reactions, tailoring smoking cessation therapies to an individual’s unique genetic inheritance.

## Glossary

**Addiction:** A chronic, relapsing disease characterized by compulsive drug seeking and abuse and by long-lasting neurochemical and molecular changes in the brain.

**Adrenal glands:** Glands located above each kidney that secrete hormones, e.g., adrenaline.

**Craving:** A powerful, often uncontrollable desire for drugs.

**Dopamine:** A neurotransmitter present in regions of the brain that regulate movement, emotion, motivation, and feelings of pleasure.

**Emphysema:** A lung disease in which tissue deterioration results in increased air retention and reduced exchange of gases. The result is difficulty breathing and shortness of breath.

**Neurotransmitter:** A chemical that acts as a messenger to carry signals or information from one nerve cell to another.

**Nicotine:** An alkaloid derived from the tobacco plant that is primarily responsible for smoking’s psychoactive and addictive effects.

**Pharmacokinetics:** The pattern of absorption, distribution, and excretion of a drug over time.

**Tobacco:** A plant widely cultivated for its leaves, which are used primarily for smoking; the *N. tabacum* species is the major source of tobacco products.

**Withdrawal:** A variety of symptoms that occur after chronic use of an addictive drug is reduced or stopped.

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## Where Can I Get More Scientific Information on Tobacco Addiction?

To learn more about tobacco and other drugs of abuse, or to order materials on these topics free of charge in English or Spanish, visit the NIDA Web site at [www.drugabuse.gov](http://www.drugabuse.gov) or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).



### What's New on the NIDA Web Site

- Information on drugs of abuse
- Publications and communications (including *NIDA Notes* and *Addiction Science & Clinical Practice* journal)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

### NIDA Web Sites

[drugabuse.gov](http://drugabuse.gov)  
[backtoschool.drugabuse.gov](http://backtoschool.drugabuse.gov)  
[smoking.drugabuse.gov](http://smoking.drugabuse.gov)  
[teens.drugabuse.gov](http://teens.drugabuse.gov)

### For Physician Information

**NIDAMED** 

[www.drugabuse.gov/nidamed](http://www.drugabuse.gov/nidamed)

### Other Web Sites

Information on tobacco addiction is also available through these other Web sites:

- Centers for Disease Control and Prevention: [www.cdc.gov/tobacco](http://www.cdc.gov/tobacco)
- National Cancer Institute: [www.cancer.gov](http://www.cancer.gov)
- U.S. Department of Health and Human Services: [www.smokefree.gov](http://www.smokefree.gov)
- Substance Abuse and Mental Health Services Administration Health Information Network: [www.samhsa.gov/shin](http://www.samhsa.gov/shin)
- Society for Research on Nicotine and Tobacco: [www.srnt.org](http://www.srnt.org)
- NicNet: [www.nicnet.org](http://www.nicnet.org)
- The Robert Wood Johnson Foundation: [www.rwjf.org](http://www.rwjf.org)
- Join Together Online: [www.quitnet.org](http://www.quitnet.org)
- American Legacy Foundation: [www.americanlegacy.org](http://www.americanlegacy.org)

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