

## Nicotine and related disorders

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## Definition

Nicotine is the main addictive ingredient in tobacco. It is a physically and psychologically addictive drug. Nicotine is the most influential drug in the United States and worldwide that produces dependence on its use, which is associated with serious health risks.

### Nicotine effects and trends

#### Effects:

- Nicotine is highly addictive.
- The tar in cigarettes increases a person's chance of developing lung cancer, emphysema, or chronic bronchitis.
- The carbon monoxide in smoke increases the risk of developing a cardiovascular disease.
- Pregnant smokers are more likely to have miscarriages or babies born with low birth weights.
- Secondhand smoke can cause lung cancer in adults and greatly increases the risk of respiratory illnesses in children.

#### Statistics and trends:

In 2008, nearly 71 million Americans aged 12 and older used a tobacco product at least once in the past month.

- Almost 60 million smoked cigarettes
- 8.7 million used smokeless tobacco
- More than 13 million smoked cigars
- Just under 2 million smoked pipe tobacco

SOURCE: National Institutes of Health, National Institute on Drug Abuse, "Tobacco/Nicotine." Available online at: <http://www.drugabuse.gov/drugpages/nicotine.html> (accessed August 16, 2010).

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## Description

Nicotine is the most addictive and psychoactive chemical in tobacco, a plant native to North America. Early European explorers learned to smoke tobacco leaves from indigenous peoples who had been using tobacco for hundreds of years. The settlers took tobacco back to Europe, where it became immensely popular. Tobacco became a major source of income for the American colonies and later for the United States. Advances in cigarette-making technology caused a boom in cigarette smoking in the early 1900s. Before the early twentieth century, most people who used tobacco did so through pipes, cigars, or chewing tobacco.

In the 1950s, researchers began to link cigarette smoking to certain respiratory diseases and cancers. In 1964, the Surgeon General of the United States issued the first health report on smoking. Cigarette smoking peaked in the United States in the 1960s and then began to decline as health concerns about tobacco increased. In 1971, cigarette advertising was banned from television, although tobacco products continued to be advertised in other media.

Pure nicotine is a colorless liquid that turns brown and smells like tobacco when exposed to air. Nicotine can be absorbed through the skin, the lining of the mouth and nose, and the moist tissues lining the lungs. Cigarettes are the most efficient nicotine delivery system. Once tobacco smoke is

inhaled, nicotine reaches the brain in less than 15 seconds. Because people who smoke pipes and cigars do not inhale, they absorb nicotine more slowly. Nicotine in chewing tobacco and snuff is absorbed through the mucous membranes lining the mouth and nasal passages. There are also several “hard snuff” and other new tobacco products being produced and marketed as alternative to traditional tobacco products. At least one study of the nicotine content of these products has found that some have lower levels of nicotine than regular tobacco products, but others contain comparable levels.

## Key Terms

### **Cold turkey**

A slang term for stopping the use of nicotine (or any other addictive drug) suddenly and completely.

### **Dopamine**

A chemical in brain tissue that serves to transmit nerve impulses and helps to regulate movement and emotions.

### **Epinephrine**

Also known as adrenaline, the hormone secreted by the adrenal glands in response to stress.

### **Neurotransmitter**

One of a group of chemicals secreted by a nerve cell (neuron) to carry a chemical message to another nerve cell, often as a way of transmitting a nerve impulse. Examples of neurotransmitters include acetylcholine, dopamine, serotonin, and norepinephrine.

### **Plaque**

A sticky cholesterol-containing substance that builds up on the walls of blood vessels, reducing or blocking blood flow.

### **Psychoactive**

Refers to a drug that affects the mind.

### **Tolerance**

A progressive decrease in the effectiveness of a drug with long-term use, requiring higher doses to achieve the desired effect.

### **Withdrawal**

Symptoms experienced by a person who has become physically dependent on a drug, experienced when the drug use is discontinued.

## Demographics

There were about 36.5 million adult smokers in the United States in 2015, which make up about 15.1% of adults who are 18 years or older.

The prevalence of smoking gradually has decreased in the United States and many other industrialized countries beginning in the 1970s, but the use of tobacco products rapidly increased in developing nations, which account for about 80% of worldwide tobacco users. The World Health Organization stated in May 2017 that tobacco kills more than 7 million people in the world each year, including more than 890,000 people who are exposed to second-hand smoke. Younger populations might be particularly vulnerable. Use of tobacco products in poor and developing countries is of particular concern, because these countries often lack adequate healthcare resources to treat smoking-related diseases, let alone support smoking cessation programs.

In the United States, men are more likely to smoke than women (25.2% of men to 15.4% of women). U.S. people who smoke tend to have less formal education than those who do not, have incomes below poverty level, and live in the South or Midwest.

Most tobacco users begin while in their teen years, although smoking declined in middle school and high school students between 2011 and 2016. More high school students are taking up electronic cigarettes than traditional cigarettes. Age breakdown of tobacco use in the United States is fairly evenly split among adult age groups, with those 25 to 44 years smoking the most. Only about 11% of older adults (65 years or older) smoke. Despite declines in tobacco use, smoking is the leading cause of preventable death in the United States: at least 480,000 deaths from smoking-related problems occur annually. Men and women who smoke in the United States are about three times as likely to die than nonsmokers.

## Causes and symptoms

### How nicotine works

Nicotine is the main addictive drug among the 4,000 chemicals found in tobacco smoke. Other substances in smoke such as tar and carbon monoxide present documented health hazards, but they are not addictive and do not cause cravings or withdrawal symptoms to the extent that nicotine does. Neuroimaging technology has shown that levels of monoamine oxidase, the enzyme responsible for boosting mood-enhancing molecule levels in the brain, increase in response to smoking, even though nicotine does not affect levels of this enzyme. Thus, some other compound in cigarette smoke must be acting to exert this effect. In addition, the compound in cigarette smoke acetaldehyde may contribute to tobacco addiction and may have a stronger effect in adolescents.

Nicotine is both a stimulant and a sedative. It is a psychoactive drug, meaning that it works in the brain, alters brain chemistry, and changes mood. Once tobacco smoke is inhaled, nicotine passes rapidly through the linings of the lungs and into the blood. It quickly circulates to the brain where it stimulates release of dopamine, a neurotransmitter (nerve signaling molecule) that affects mood. Drugs that elicit an increase in dopamine influence the brain's reward pathway, causing the user to turn again to the drug for another pleasurable, rewarding dopamine response. This release accounts for the pleasurable sensation that most smokers feel almost as soon as they light a cigarette.

As nicotine affects the brain, it also stimulates the adrenal glands. The adrenal glands are small, pea-sized organs located above each kidney that act as two different endocrine organs. The adrenal gland produces several hormones in the medulla, or inner layer, including epinephrine, also called adrenaline. Under normal circumstances, adrenaline is released in response to stress or a perceived threat. It is sometimes called the fight-or-flight hormone, because it prepares the body for action. When adrenaline is released, blood pressure, heart rate, blood flow, and oxygen use increase. Glucose, a simple form of sugar used by the body, floods the body to provide extra energy to muscles. The overall effect of the release of the stress hormones is strain on the cardiovascular (heart and blood vessels) system. This response to stress produces inflammation in the blood vessels that ultimately results in buildup of plaque, which can block the vessels and cause stroke or heart attack.

Research suggests that there might be a genetic component to nicotine dependence, just as there is for alcohol dependence. A 2017 report showed that a common variant, or change, in DNA could lead to dependence. Researchers found the gene variant in nearly half of people of European descent and nearly three-fourths of African Americans.

Most people begin smoking between the ages of 12 and 20. Few people start smoking as adults older than 21. Adolescents who smoke tend to begin as casual smokers, out of rebellion or a perceived need for social acceptance. Dependence on nicotine develops rapidly, however; one study suggests that 85%–90% of adolescents who smoke four or more cigarettes become regular smokers. Nicotine is addictive, so being tobacco-free soon feels uncomfortable for users. In addition, smokers quickly develop tolerance to nicotine. Tolerance is a condition that occurs when the body needs a larger and larger dose of a substance to produce the same effect. For smokers, tolerance to nicotine means more

frequent and more rapid smoking. Soon most smokers develop physical withdrawal symptoms when they try to stop smoking. Users of other forms of tobacco experience the same effects; however, the delivery of nicotine is slower and the effects may not be as pronounced.

## Nicotine dependence

In addition to the physical dependence caused by the actions of nicotine on the brain, there is a strong psychological component to the dependency of most users of tobacco products, especially cigarette smokers. Most people who start smoking or using smokeless tobacco products do so because of social factors. These include:

- desire to fit in with peers
- acceptance by family members who use tobacco
- rebelliousness
- association of tobacco products with maturity and sophistication
- positive response to tobacco advertising

Personal factors such as mental illness (depression, anxiety, schizophrenia, or alcoholism), the need to reduce stress and anxiety, or a desire to avoid weight gain also influence people to start smoking. Once smoking has become a habit, whether physical addiction occurs or not, psychological factors play a significant role in a person's continuing to smoke. People who want to stop smoking might be discouraged from doing so because of the following:

- living or working with people who smoke and who are not supportive of their quitting
- believing they are incapable of quitting
- perceiving no health benefits to quitting
- having tried to quit before and failed
- associating cigarettes with specific pleasurable activities or social situations that they are not willing to give up
- fear of gaining weight

Successful smoking cessation programs must treat both the physical and psychological aspects of nicotine addiction.

## Nicotine withdrawal

The American Psychiatric Association first recognized nicotine dependence and nicotine withdrawal as serious psychological problems in 1980. The Centers for Drug Control and Prevention states that nicotine could be as addictive as illegal drugs such as cocaine and heroin. Quitting nicotine can be difficult. Among people who try, between 75% and 80% relapse within six months. Because of this rate, research has found that smoking cessation programs that last longer than six months can greatly enhance quit rates, achieving rates as high as 50% at one year. Combining a nicotine-withdrawal product with a behavioral-modification or support program has produced the greatest success rates.

The combination of physiological and psychological factors make withdrawal from nicotine very difficult. Symptoms of nicotine withdrawal include:

- irritability
- restlessness
- increased anger or frustration
- sleep disturbances
- inability to concentrate
- increased appetite or desire for sweets
- depression

- anxiety
- constant thoughts about smoking
- cravings for cigarettes
- decreased heart rate
- coughing

Withdrawal symptoms are usually more pronounced in smokers than in those who use smokeless tobacco products, and heavy smokers tend to have more symptoms than light smokers when they try to stop smoking. People with depression, schizophrenia, alcoholism, or mood disorders may find it especially difficult to quit, as nicotine offers temporary relief for some of the symptoms of these disorders.

Symptoms of nicotine withdrawal begin rapidly and peak within one to three days. Withdrawal symptoms generally last three to four weeks, but a significant number of smokers have withdrawal symptoms lasting longer than one month. Some people have strong cravings for tobacco that last for months, even though the physical addiction to nicotine is gone. These cravings often occur in settings in which the person formerly smoked, such as at a party, while driving, or after a meal. Researchers believe that much of this extended craving is psychological.

## Diagnosis

Smokers usually self-diagnose their nicotine dependence and nicotine withdrawal. Such questionnaires as the Fagerstrom Test for Nicotine Dependence (FTND), a short six-item assessment of cigarette use, help to determine the level of tobacco dependence. Physicians and mental health professionals are less concerned with diagnosis, which is usually straightforward, than with determining the physical and psychological factors in each patient that must be addressed for successful smoking cessation.

The Diagnostic and Statistical Manual of Mental Disorders, fifth edition, the handbook used by medical professionals in diagnosing mental health conditions, recognizes nicotine addiction. The manual also recognizes tobacco use disorder as a substance abuse disorder. The criteria for diagnosing a tobacco use disorder are similar to any substance abuse disorder. A total of 11 nicotine addiction criteria include persistent desire or unsuccessful efforts to quit, cravings, giving up important social or recreational activities because of smoking, continued use of tobacco despite knowledge of its effect on one's personal or physical health, repeated use of tobacco in hazardous situations such as smoking in bed.

## Treatment

Most people do not decide to stop smoking suddenly. Instead, they go through several preparatory stages before taking action. First is the precontemplation stage, in which the smoker does not even consider quitting. Precontemplation is followed by the contemplation stage, in which the smoker thinks about quitting but takes no action. Contemplation eventually turns to preparation, often when counselors or family members encourage or urge the smoker to quit. Now the smoker starts making plans to quit soon. Finally the smoker arrives at the point of taking action.

Having decided to stop smoking, a person has many choices of programs and approaches. When mental health professionals are involved in smoking cessation efforts, one of their first jobs is to identify the physical and psychological factors that keep the person smoking. This identification helps to direct the smoker to the most appropriate type of program. Assessment examines the frequency of the person's smoking, social and emotional attachment to cigarettes, commitment to change, available support system, and barriers to change. These conditions vary from person to person, which is why some smoking cessation programs work for one person and not another.

## Education

Education is a critical part of treatment for nicotine addiction. Smokers and other tobacco users are made aware of the benefits of quitting, what to expect from the nicotine withdrawal process, and therapies and products available to help quit.

## Medications

Before 1984, there were no medications to help smokers quit. In that year, a nicotine chewing gum (Nicorette) was approved by the U.S. Food and Drug Administration (FDA) as a prescription drug for smoking cessation. In 1996, it became available without prescription. Nicorette was the first of several medications used for nicotine replacement therapy, intended to gradually reduce nicotine dependence to prevent or reduce withdrawal symptoms. This approach, called tapering, is used in withdrawal of other addictive drugs. Studies indicate that people using these replacement therapies do not become addicted to them.

Nicotine replacement therapy comes in the form of gum, inhalers, nasal sprays, lozenges, and a skin patch. As a gum is chewed or a lozenge is sucked, nicotine is released and absorbed through the lining of the mouth. Over a 6- to 12-week period, the amount and strength of the nicotine replacement product can be decreased until the smoker is weaned away from dependence on nicotine. People trying to quit smoking are instructed to use the gum, spray, or lozenges when they feel a craving. All nicotine replacement therapy is more effective when combined with education or counseling.

Nicotine transdermal patches became available without prescription in 1996. They are marketed under several brand names, including NicoDerm CQ, Nicotrol, and Habitrol. The patches are worn on the skin between the neck and the waist and provide a steady delivery of nicotine through the skin. Some brands are worn for 24 hours, and some for 16 hours at night. The patches come in varying strengths, and after several weeks, users can switch to a patch that delivers a lower dose. Some people using the 24-hour patches experience sleep disturbances, and a few develop mild skin irritations, but generally side effects are few. Doctors recommend not smoking while using the patch and moving the patch to a different area each time it is replaced.

As of 2017, nicotine replacement gum and lozenges were available without a prescription. Patches also are available without a prescription, although a person wanting to quit can get a prescription from a health care provider. Nicotine nasal sprays and inhalers require a prescription. These products deliver nicotine rapidly, just as a cigarette does, but at a much lower dose than a cigarette. Side effects include cold-like symptoms (runny nose, sneezing, etc.). A nicotine inhaler was also available that delivers nicotine through the tissues of the mouth. A major advantage of the inhaler is that it provides an alternative to having a cigarette in one's hands while still delivering nicotine. It delivers less nicotine in cold weather (under 50°F). Sprays can be used along with patches when people begin efforts to quit tobacco.

Prescription drugs outside of nicotine replacement therapy have been approved for the treatment of nicotine dependence. The first-approved drug was bupropion (Zyban), an antidepressant that acts to cut down withdrawal symptoms. This drug can be used in combination with a nicotine replacement therapy and behavioral therapy.

A newer drug is varenicline (Chantix), which was developed to help people stop smoking. This drug acts directly on the proteins in the brain that recognize and bind nicotine. Interfering with their action not only stops the brain from sending the pleasurable message of nicotine but also reduces the feelings of nicotine withdrawal. Some studies indicate that this drug can double a person's chances of quitting smoking. Side effects of this drug can include headache, nausea, vomiting, sleep problems, gas, and changes in taste sensation.

Other drugs used in some smoking cessation programs include nortriptyline (Pamelor), a tricyclic antidepressant, and clonidine (Catapres), a high blood pressure medication. Side effects of these drugs include dry mouth and drowsiness. Both of these drugs are second-line treatments (used only when other treatments have shown no results) and are considered off-label uses (not approved by the FDA for this purpose).

## Behavioral therapy

Behavioral treatments are used to help smokers learn to recognize and avoid specific situations that trigger desire for a cigarette. They also help the smoker learn to substitute other activities for smoking. Behavioral treatments are almost always combined with smoker education, and they usually involve forming a support network of other smokers who are trying to quit.

Behavioral treatments often take place in support groups either in person or online. They are most effective when combined with nicotine replacement therapy. Other supportive techniques include the use of rewards for achieving certain goals and contracts to clarify and reinforce the goals. Overall, quit rates are highest when behavior modification is combined with nicotine replacement therapy and tapering. Behavioral approaches are available in person, via mail, telephone, apps, and online for greater access and flexibility. The U.S. Department of Health and Human Services sponsors a toll-free number for people who want to quit. This number serves as the point of contact for smokers who want information and help.

## Alternatives

Many alternative therapies have been tried to help smokers withdraw from nicotine. Hypnosis has proved helpful in some cases but has not been tested in controlled clinical trials. Acupuncture, relaxation techniques, restricted environmental stimulation therapy (REST, a combination of relaxation and hypnosis techniques), special diets, and herbal supplements have all been used to help people stop smoking. Of these alternative techniques, clinical studies of REST showed substantial promise in helping people stop smoking permanently.

## Prognosis

Smoking is a major health risk associated with nicotine dependence. Tobacco use is considered the leading preventable cause of death in the United States. An estimated 480,000 tobacco users in the United States die each year—more than alcohol, illegal drug, homicide, suicide, car accidents, and HIV rates combined. Of those 480,000, about 40% die from cancer, 35% from heart disease and stroke, and 25% from lung disease. Most lung cancers, the leading cause of cancer death in the United States, are linked to smoking, and smoking is linked to about one-third of all cancer deaths. Smoking also causes such other lung problems as chronic bronchitis and emphysema, as well as worsening the symptoms of asthma. Other cancers associated with smoking include cancers of the mouth, esophagus, stomach, kidney, colon, and bladder. Smoking accounts for a large percentage of cardiovascular deaths and significantly increases the risk of heart disease, heart attack, stroke, and aneurysm. Women who smoke during pregnancy have more miscarriages, premature babies, and low-birth weight babies than nonsmokers. In addition, there is an increased risk that a child born to a mother who smokes will die of sudden infant death syndrome (SIDS), making smoking an avoidable factor in this tragic occurrence. Secondhand smoke also endangers the health of nonsmokers in the smoker's family or workplace. Although most of these effects are not caused directly by nicotine, it is the dependence on nicotine that keeps people smoking.

Even though it is difficult for smokers to break their chemical and psychological dependence on nicotine, most of the negative health effects of smoking are reduced or reversed after quitting.

Therefore, it is worth trying to quit smoking at any age, regardless of the length of time a person has had the habit.

## Mental health problems

Persons with mental health problems, such as depression, anxiety, and schizophrenia, are two to three times more likely to smoke than persons without these conditions. However, smoking has also been associated with the risk of developing mental health problems, which has prompted some researchers to wonder whether smoking is a causal factor in mental illnesses or just prevalent due to effects of nicotine.

## Prevention

The best way to avoid nicotine dependence and withdrawal is to avoid the use of tobacco products. In September 2012, the FDA started requiring all cigarette manufacturers to display large, pictographic warning labels on cigarette packaging to deter consumers from purchasing cigarettes. The labels feature images focused on the negative effects of smoking, such as damaged lungs, oral cancer, children affected by secondhand smoke, and even a deceased person. The goal of the new labels was to both help current smokers quit smoking and to prevent others from starting smoking. Public health efforts often focus on keeping adolescents from starting smoking.

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## Organizations

American Cancer Society Street 250 Williams St. NW Atlanta GA 30303 Free (800) 227-2345  
<http://www.cancer.org>

American Lung Association Street 55 Wacker Drive, Suite 1150 Chicago IL 60601 Free (800) 586-4872 [info@lungusa.org](mailto:info@lungusa.org) <http://www.lungusa.org>

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