Nicotine

For thousands of years, people have smoked or chewed the leaves of the tobacco plant, *Nicotiana tabacum*. Tobacco was first found and cultivated in the Americas, perhaps as early as 6000 B.C. Following the discovery and colonization of North and South America, the tobacco plant was exported widely, to continental Europe and the rest of the civilized world. Even in its early days, tobacco use was controversial. Some hailed its medicinal properties. For example, tobacco was supposed to be protective against the ravages of the Plague! As early as the 1600s, people speculated that there might be a link between diseases, like cancer and tobacco use. Since then, modern research methods have provided evidence of this link, and public service announcements that warn of tobacco's health risks and addictive nature are seen regularly on TV.

What is it about tobacco that makes people so compelled to use it despite all of the admonitions? Smoking or chewing tobacco makes people feel good, even mildly euphoric. While there are thousands of chemicals in the tobacco plant (not to mention those added by cigarette manufacturers), one, **nicotine**, produces all the good feelings that draw people back for another cigarette or plug of tobacco.

Nicotine ($C_{10}H_{14}N_2$) is a naturally occurring **liquid alkaloid**. An alkaloid is an organic compound made out of carbon, hydrogen, nitrogen and sometimes oxygen. These chemicals have potent effects on the human body. For example, many people regularly enjoy the **stimulating** effects of another alkaloid, caffeine, as they quaff a cup or two of coffee in the morning.

Nicotine normally makes up about 5 percent of a tobacco plant, by weight. Cigarettes contain 8 to 20 milligrams (mg) of nicotine (depending on the brand), but only approximately **1 mg is actually absorbed** by your body when you smoke a cigarette.

Nicotine in the Body

As with most addictive substances, humans have devised a number of ways of delivering nicotine to their bodies. Nicotine readily **diffuses** through:

- **Skin**
- **Lungs**
- **Mucous membranes** (such as the lining of your nose or your gums)

Nicotine moves right into the small blood vessels that line the tissues listed above. From there, nicotine travels through your bloodstream to the brain, and then is delivered to the rest of your body.
The most common (and the most expedient way) to get nicotine and other drugs into your bloodstream is through **inhalation** -- by smoking it. Your lungs are lined by millions of alveoli, the tiny air sacs where gas exchange occurs. These **alveoli** provide an enormous surface area -- 90 times greater than that of your skin -- and thus provide ample access for nicotine and other compounds. Once in your **bloodstream**, nicotine flows almost immediately to your **brain**. Although nicotine takes a lot of different actions throughout your body, what it does in the brain is responsible for both the good feelings you get from smoking, as well as the irritability you feel if you try to quit (see the section on addiction and withdrawal for details). Within 10 to 15 seconds of inhaling, most smokers are in the throes of nicotine's effects.

Nicotine doesn't stick around your body for too long. It has a half-life of about 60 minutes, meaning that six hours after a cigarette, only about 0.031 mg of the 1 mg of nicotine you inhaled remains in your body.
How does your body get rid of nicotine? Here's the process:

- About 80 percent of nicotine is broken down to cotinine by enzymes in your liver.
- Nicotine is also metabolized in your lungs to cotinine and nicotine oxide.
- Cotinine and other metabolites are excreted in your urine. Cotinine has a 24-hour half-life, so you can test whether or not someone has been smoking in the past day or two by screening his or her urine for cotinine.
- The remaining nicotine is filtered from the blood by your kidneys and excreted in the urine.

Different people metabolize nicotine at different rates. Some people even have a **genetic defect** in the enzymes in their liver that break down nicotine, whereby the mutant enzyme is much less effective at metabolizing nicotine than the normal variant. If a person has this gene, their blood and brain nicotine levels stay higher for longer after smoking a cigarette. Normally, people keep smoking cigarettes throughout the day to maintain a steady level of nicotine in their bodies. Smokers with this gene usually end up smoking many fewer cigarettes, because they don't constantly need more nicotine.

How Nicotine Works

Nicotine and the Brain.

Your brain is the key player in nicotine's action. Like a computer, your brain processes, stores and uses information. In a computer, information travels in the form of electricity moving through wires; information transfer is a binary process, with switches being either "on" or "off." In your brain, **neurons** are the cells that transfer and integrate information. Each neuron has thousands of inputs from other neurons throughout the brain. Each of these signals is included in the calculation of whether or not the neuron will pass the signal it receives on to other neurons in the pathway.

While signals are conducted through individual neurons as electric current, communication between neurons is mediated by chemical messengers, called **neurotransmitters**. Neurotransmitters traverse the physical space between two neurons and bind to special protein receptors on the postsynaptic cell. Once bound, these receptors set in motion physiological changes within the neuron that allow it to send the signal on down the line.

Each neurotransmitter has its own specific family of receptors. Nicotine works by docking to a subset of receptors that bind the neurotransmitter **acetylcholine**. Acetylcholine is the neurotransmitter that (depending on what region of the brain a neuron is in):

- Delivers signals from your brain to your muscles
- Controls basic functions like your energy level, the beating of your heart and how you breathe
- Acts as a "traffic cop" overseeing the flow of information in your brain
- Plays a role in learning and memory

Like acetylcholine, nicotine leads to a burst of receptor activity. However, unlike acetylcholine, nicotine is not regulated by your body. While neurons typically release small

amounts of acetylcholine in a regulated manner, nicotine activates cholinergic neurons (which mainly use acetylcholine to communicate to other neurons) in many different regions throughout your brain simultaneously. This stimulation leads to:

- **Increased release of acetylcholine** from the neurons, leading to heightened activity in cholinergic pathways throughout your brain. This cholinergic activity calls your body and brain to action, and this is the wake-up call that many smokers use to re-energize themselves throughout the day. Through these pathways, nicotine improves your reaction time and your ability to pay attention, making you feel like you can work better.
- **Stimulation of cholinergic neurons** promotes the release of the neurotransmitter dopamine in the **reward pathways** of your brain - This neural circuitry is supposed to reinforce behaviors that are essential to your survival, like eating when you're hungry. Stimulating neurons in these areas of the brain brings on pleasant, happy feelings that encourage you to do these things again and again. When drugs like cocaine or nicotine activate the reward pathways, it reinforces your desire to use them again because you feel so at peace and happy afterwards.
- **Release of glutamate**, a neurotransmitter involved in learning and memory - Glutamate enhances the connections between sets of neurons. These stronger connections may be the physical basis of what we know as memory. When you use nicotine, glutamate may create a **memory loop** of the good feelings you get and further drive the desire to use nicotine.

Nicotine also increases the level of other neurotransmitters and chemicals that modulate how your brain works. For example, your brain makes more **endorphins** in response to nicotine. Endorphins are small proteins that are often called the body's natural pain killer. It turns out that the chemical structure of endorphins is very similar to that of heavy-duty synthetic painkillers like morphine. Endorphins can lead to feelings of euphoria also. If you're familiar with the runner's high that kicks in during a rigorous race, you've experienced the "endorphin rush." This outpouring of chemicals gives you a mental edge to finish the race while temporarily masking the nagging pains you might otherwise feel.

For more information visit

http://science.howstuffworks.com/nicotine.htm