Can Reducing Nicotine Help Wean Smokers?

By Mary Beckman

The tobacco industry has admitted outright, and now researchers and health care professionals are taking it to heart: Cigarettes are a nicotine delivery system.

The trouble is that nicotine itself isn’t all that bad for you. In fact, some research suggests it could help schizophrenia, attention deficit disorder, and depression, as well as the average Joe who just wants to focus a little better.

And cigarette smoke is an effective courier. Breathing in naked nicotine hurts the lungs, and as odd as it seems to nonsmokers, cigarette smoke actually smoothes nicotine inhalation. From the lungs, nicotine has a straight shot to the brain. Taking in the addictive drug through other routes doesn’t feel the same, nor does it act as quickly.

But cigarette smoke is full of a myriad of chemicals known to cause cancer. Because tobacco smoke causes so much disease, public-health professionals and organizations are more concerned with getting people off the smoke than they are with getting people off nicotine. To that end, researchers have been testing whether changing nicotine levels in tobacco would make people lose interest in smoking, and the data aren’t at all clear.

In March, U.S. Food and Drug Administration Commissioner Andrew von Eschenbach, M.D., weighed in on the debate, saying that regulating tobacco to contain less nicotine could backfire and cause people to smoke even more to get their fix. But experts say it’s too early to know what would happen with regulated nicotine levels in tobacco.

“I think because of the health problems and disease and death related to smoking, any well-designed study to test these ideas deserves consideration,” says smoking behavior researcher Andrew Strasser, Ph.D., of the University of Pennsylvania.

The Push To Regulate

Clinical pharmacologist Neal Benowitz, M.D., at the University of California, San Francisco, has been pushing for lower levels of nicotine in tobacco since the early 1990s, both to help smokers quit and prevent new users from becoming lifelong smokers.

“If you remove nicotine from tobacco and do it gradually, it may be possible to reduce nicotine dependence, so when adolescents first start smoking, they won’t become addicted,” he says. But the data appear to point in contradictory directions. Some show that when people smoke lower-nicotine “light” cigarettes, they take bigger, longer puffs. Yet other studies show that sometimes people do not inhale more to compensate when their cigarette has less nicotine.

“The jury’s still out,” says nicotine researcher Jed Rose, Ph.D., of Duke University Medical Center in Durham, N.C. “The tentative conclusion that’s emerging is if nicotine is reduced but not the tar level, then there will be some but not a huge amount of compensation.”

This might be because people smoke cigarettes for the flavor of the tar and other smoke components but become addicted because of the nicotine. As long as people feel like they’re smoking like they always have, they might not notice incremental drops in nicotine, he says.

Strasser isn’t convinced. He says there are “quite a large amount of data” that show that with decreased nicotine levels people will smoke more intensely or will smoke more cigarettes every day. But he adds that the magnitude of the drop in nicotine levels might be an important factor in whether smokers compensate, and that should be looked at more closely.

Modified Filters, Modified Plants

What’s partly contributing to the debate, Benowitz says, is how companies make low-nicotine cigarettes. Nearly all light cigarettes on the market have filters packed with tiny vents that allow more air into the airstream created when someone puffs on it. Adding air to the inhaled smoke dilutes the nicotine as well as the harmful smoke components. Commercial cigarettes are graded by machine testing, and the vents allow the cigarettes to pass as a lower-nicotine and lower-tar product. Some smokers are unaware of the vents; others block them with tape, Strasser says.

In a 2005 study in Pharmacology, Biochemistry, and Behavior, Strasser and colleagues suggested that blocking the vents of light cigarettes negates any benefit that the lower nicotine cigarettes might provide. Asked to puff on a Marlboro or Carlton cigarette eight times for 45 seconds each, the volunteers sucked in significantly more smoke when puffing on the ultralight cigarettes with the filter vents completely open. When smokers could puff for as long as they liked, they puffed longer on light or...
ultralight cigarettes than on normal cigarettes, suggesting that these smokers are compensating for the lower delivery.

Also, partly blocking the vents resulted in people breathing in much more carbon monoxide than when the vents were unblocked. This finding suggests that rather than reducing harm by reducing nicotine intake, smokers who compensate are putting themselves at greater risk of hazardous chemicals, Strasser says.

But there are other ways of reducing the nicotine in tobacco smoke besides the vents. Chemists can extract the nicotine directly, and geneticists have been developing tobacco plants that make less nicotine. In a 2006 study in Clinical Pharmacology and Therapeutics, Benowitz and colleagues used a series of cigarettes with decreasing amounts of nicotine to evaluate whether volunteers compensate for low nicotine content. The non–commercially available cigarettes were made by mixing nicotine-extracted tobacco with regular tobacco to achieve nicotine levels ranging from 1 mg to 12 mg of nicotine per cigarette (the researchers determined the actual values experimentally, which were slightly lower than the target levels). The 12-mg cigarette was comparable in nicotine content to the usual brand that the volunteers smoked, which was also included in the samples of cigarettes in the experiment.

Although the measured content of nicotine in the experimental cigarettes ranged from 0.6 mg to 10 mg, the tar levels remained the same. Unlike Strasser’s filter vent study, Benowitz did not find that smokers compensated by inhaling more, from the amount of nicotine found in blood samples. Nor did the researchers find that volunteers took in more carbon monoxide with the lower-nicotine cigarettes.

Another Strasser study, published this year in Drug and Alcohol Dependence, examined whether commercially available cigarettes (specifically the Qwest brand) produced with tobacco genetically altered to contain less nicotine prompted smokers to puff harder and longer. The nicotine amounts were much lower than the standard cigarette—from 0.6 mg per cigarette to 0.05 mg—and all contained equivalent levels of tar. People took in more smoke when puffing on a 0.05-mg cigarette than a 0.3-mg cigarette, and they sucked in more carbon monoxide with a 0.3-mg cigarette than with a 0.6-mg cigarette. But the increases were smaller than with the filter-vented lights. “People will still try to smoke these cigarettes more intensely,” Strasser says. He adds that the experiment did not address whether smokers would go through more cigarettes a day to compensate for the lower nicotine levels.

Duke’s Rose suggests that at a minimum, lower-nicotine cigarettes will help people who want to quit do so more successfully. In a 2006 Nicotine and Tobacco Research study, Rose showed that about 20% to 30% of smokers using low-nicotine cigarettes to quit remained non-smokers at 4 weeks, compared to about 10% of smokers using regular cigarettes.

But some scientists’ goals reach higher than just allowing smokers to quit on their own. “Most smokers would like to be weaned from their addiction,” Benowitz says. “Most adolescents do not want to become adult smokers. They think they’ll be able to quit in a year or two.” He is working toward his dream of cigarettes eventually having a nicotine level so low that most people won’t become addicted in the first place. Strasser points out other research that seeks a nicotine delivery system that doesn’t rely on cancer-causing smoke but is just as effective—such as nasal sprays.

“I would envision making nicotine replacement therapies easy to get, while phasing out nicotine from cigarettes so smoke doesn’t get linked with nicotine usage,” Rose says. “Right now it’s just the opposite. The clean nicotine is hard to get and it’s easy to get the cancer-causing one.”

Left to its own devices, the tobacco industry does not appear to want to wean people off their delivery systems: A report from the Harvard School of Public Health shows that nicotine levels in major brands of cigarettes rose 11% from 1998 to 2005, based on standardized machine testing of cigarettes. Such data cause public-health professionals to call for the government to regulate nicotine.

“Unfortunately, it is the tobacco industry that best understands how nicotine levels can be titrated to produce human addiction. This topic area is usually shrouded in secrecy, hidden from public scrutiny,” says Howard Koh, coauthor of the Harvard report and associate dean for public health at Harvard University. “Consumers and the general public deserve much more information.”

The researchers say that more studies examining when and how people compensate for lower nicotine could set the stage for weaning on a large scale, and Benowitz says the first step is to wrest control of nicotine levels from the tobacco companies. “Federal regulation is the most effective way to move forward,” Benowitz says. He says von Eschenberg might not be aware of the research showing cases in which people don’t compensate because it hasn’t been published yet. “It’s really important for developing a sustained plan for reducing tobacco use and maintaining surveillance.”

In February, two senators and two representatives introduced congressional legislation called the Family Smoking Prevention and Tobacco Control Act, a bill that would give the FDA power to regulate tobacco products. One tobacco company, Philip Morris, supports the legislation.

A second coauthor of the Harvard report, professor of public health Gregory Connolly of Harvard, says that reducing nicotine could be done with as much care as the U.S. controlled opium and cocaine in the early 1900s. He backs a plan to reduce levels of nicotine, “one of the most powerful drugs known in our society.

“If we got the levels in cigarettes down to that of tomatoes (0.3 mg/g), we wouldn’t have people outside of buildings smoking cigarettes,” he says. “When was the last time you saw a person outside of a building eating a bag of tomatoes?”