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# NICOTINE: A DRUG OF CHOICE?

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## More than 20 years after the U.S. Surgeon General first indicted tobacco as a health hazard, new research suggests habitual nicotine use causes a true drug dependency

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By DIANE D. EDWARDS

**H**aving resolved to make 1986 smoke-free, some people will try this month to avoid their usual smoky haunts; others will seek diversions from lighting up the next cigarette. Motivation for many will be the scientific data linking tobacco smoking to heart and lung disease and to cancer. According to George Bigelow, associate professor of behavioral biology at Johns Hopkins School of Medicine in Baltimore, there are 350,000 smoking-related deaths in the United States each year—making the daily toll equivalent to that of four airplane crashes of the size of the one that took place Dec. 12 at Gander, Newfoundland.

"Because [smoking] is socially acceptable, we've become inured to the true magnitude of this health problem," Bigelow told an American Psychological Association science forum last month in Washington, D.C. "Beyond the loss of life and human misery is the cost in terms of dollars . . . an estimated \$39 billion to \$96 billion annually [including loss of productivity and \$25 billion in medical costs]." Why, with growing evidence of the dangers and high costs of smoking, are more than 50 million Americans smoking cigarettes?

Tobacco industry representatives cite personal choice as the primary reason people continue to smoke. Yet, for the multitude of U.S. tobacco smokers who will try to kick their habit this year (16 million tried in 1980, the most recent estimate), quitting may involve more than the psychological battles of mind over matter, or fears for health over the pleasures of smoking. As reported in the U.S. Surgeon General's latest study on tobacco and health, released last month, a 1980 study found that 60 percent of U.S. smokers had seriously tried to stop smoking. But more than 80 percent who try relapse within the year (see graph)—many the victims of what recent scientific evidence suggests is actual physical dependency.

**S**cientists and smokers have long suspected that nicotine, not just the act of smoking, is somehow addictive. But it wasn't until the late 1970s that rigorous experimentation on the addiction theory began, raising questions of how any acceptance of nicotine as a habit-forming drug would affect legislation and litigation. Subsequent research compared the patterns and effects of habitual nicotine use with addiction to drugs like heroin and amphetamines. Results from some of that research were reported last month at a symposium on the neurobiologic aspects of tobacco smoking held at the University of Kentucky in Lexington.

"The role of nicotine in impulsive tobacco use is the same as the role . . . of cocaine in compulsive coca leaf use," Jack Henningfield of the Baltimore-based Addiction Research Center of the National Institute of Drug Abuse (NIDA) told SCIENCE NEWS. "We can substitute intravenous nicotine for tobacco in cigarettes and [get the same reaction] from humans and animals. The drug [nicotine] itself is critical." Nicotine, he says, meets the technical criteria of an addictive drug in laboratory studies by affecting brain wave function, altering mood and serving as a biological reward that elicits certain behavior from both laboratory animals and human volunteers.

Nicotine also appears to have certain beneficial side effects, which could partially explain the urgent craving for a smoke. Unpublished data presented at the Lexington symposium by Henningfield and other researchers agree with some of the therapeutic effects espoused by smokers.

Testing concentration, short-term memory and other cognitive skills, Henningfield's group found that 20 smokers who quit for 10 days showed significantly slower and poorer test performance within eight hours after the last cigarette. Smoking or nicotine gum restored cognitive skills, the improvement and de-

cline of which corresponded to recorded changes in electrical activity of the brain. "The effect is real, it's physical," Henningfield says. "We can measure it in the lab, but we're a long way from completely understanding it." He adds that the final consensus among the 300 symposium participants was that "clearly there are cognitive performance changes during abstinence," but the controversy over whether nicotine similarly affects non-smokers remained unresolved.

**N**onsmokers were included in research done at the University of Reading, Whiteknights, in Reading, England, where studies of nicotine and mental capabilities by psychologists Keith Wesnes and David Warburton are supported by both the British tobacco industry and public funds. Warburton told those attending the symposium that his study of 1,000 smokers found a 15 percent improvement in concentration during smoking, and another study of 30 smokers and 30 nonsmokers showed an 8 percent improvement in both groups right after smoking or taking nicotine tablets. Wesnes, who presented new data that showed cognitive improvements persist up to 30 minutes after smoking, speculates that nicotine might stimulate the cholinergic neurotransmitter system. The same system evidently is inhibited in the memory-disturbing Alzheimer's disease.

The fact that cognitive skills take time to diminish following nicotine use raises questions about the rate of nicotine elimination, the subject of recent work by others at the Kentucky conference. Using a smoking-exposure room, Dan Sepkovic of the American Health Foundation in Valhalla, N.Y., exposed volunteers to passive smoke (that not inhaled through a cigarette or pipe) for 80 minutes twice daily for 40 days, in a study funded by the National Cancer Institute. Catheters inserted in the arms of eight smokers, three never-smokers and one former

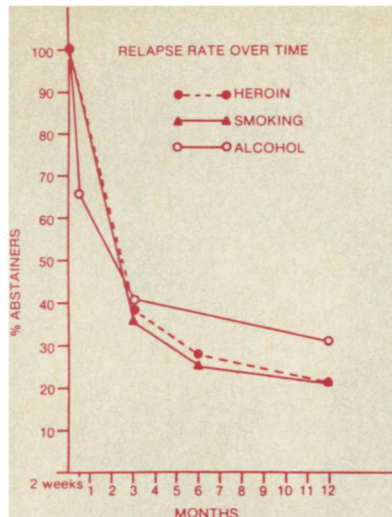
smoker collected continuous blood samples. These were assayed along with urine and saliva samples for levels of cotinine, a breakdown product of nicotine metabolism.

The rate of cotinine removal was "substantially lower" in nonsmokers than in smokers, Sepkovic told SCIENCE NEWS. In the blood, the half-life of cotinine was 20 hours in smokers and 42 hours in nonsmokers. Sepkovic had previously found a 67-hour cotinine half-life in babies (SN: 5/12/84, p. 296). He thinks that, although nonsmokers may inhale less nicotine because passive smoke from a cigarette is diluted in the air, the persistence of cotinine in their bodies may indicate that hazardous by-products of tobacco linger longer in nonsmokers. Another Sepkovic study found that rats exposed to cigarette smoke have higher levels of nicotine oxides that "readily" convert back to nicotine in the body. Sepkovic speculates that the oxides may form a nicotine reserve that stimulates craving.

Persistence of nicotine in the body of a smoker may cause lingering effects during nonsmoking times like sleep, according to Neil Benowitz, an associate professor of medicine at the University of California in San Francisco (UCSF). A smoker's daytime heart rate is, on average, 8 to 10 beats per minute higher than a nonsmoker's. Even during sleep, the average smoker's heart rate is 3 to 5 beats per minute higher than a nonsmoker's rate; it returns to the nonsmoker's levels only around 8 a.m. "One of my hypotheses is that the toxic consequences are really a result of this 24-hour exposure to things like nicotine and tar," Benowitz told SCIENCE NEWS. He says his observational study of 22 volunteers is the first directly tying nicotine elimination rates to the amount someone smokes: There is a three- to fourfold variability in the amount individuals smoke, and in the UCSF study the faster a subject metabolized nicotine the more cigarettes he or she wanted to smoke.

Furthermore, when 10 other UCSF study subjects were given ammonium chloride to increase kidney excretion of nicotine sixfold, they compensated by smoking about 20 percent more cigarettes, Benowitz says. He found similar attempts to compensate in smokers using the ultra-low-tar cigarettes, from which smokers absorb only half the tar and nicotine absorbed from regular and low-tar types. This self-regulation of nicotine levels may be more evidence that nicotine leads to physical dependence.

However, when the case of tobacco's effect on health enters the courtroom, the critical issue of whether nicotine is really a physically addictive drug is far from being resolved. The definition of "addiction" has become so broad as to be almost worthless, says one official at the U.S. Surgeon General's Of-



Relapse rates for individuals treated for heroin, smoking and alcohol addiction are very similar.

Office in Washington, D.C. Nonetheless, more than 35 personal injury lawsuits have been filed in recent years against the tobacco industry.

On Dec. 13, a federal judge in Knoxville, Tenn., dismissed the first of the latest wave in tobacco lawsuits — a \$55 million liability suit brought against R.J. Reynolds Tobacco Co. by a man who claimed cigarettes had caused the decreased circulation that forced amputation of his leg. Attorney Robert Campbell, who represented the tobacco company, told SCIENCE NEWS that "the question of personal choice was a paramount issue [in this case], and that translates into the issue of whether or not the product is defective and unreasonably dangerous in legal terminology."

In Santa Barbara, Calif., a jury similarly rejected claims in a wrongful death suit against Reynolds. The \$1 million suit was brought by the survivors of a smoker who, according to the plaintiffs' lawyers, had been addicted to cigarettes. The jury's decision on Dec. 23 followed defense summation remarks that the man "smoked because he loved it. No one forced him to smoke. Nobody put a gun to his head. It was his right, as it was anyone's right."

Because "personal choice" includes choosing from advertised products, the American Medical Association (AMA) House of Delegates adopted a controversial proposal Dec. 10 calling for a total ban of tobacco advertising. Critics quickly insisted such a ban would violate First Amendment rights, pointing out that tobacco is not an illegal drug. The AMA policymakers also agreed to support a 21-year minimum age for buying cigarettes and other tobacco products, a ban on vending-machine cigarette sales and a requirement for health warning la-

bels on smokeless tobacco, according to an AMA spokesperson. The proposals are part of the organization's effort to improve chances of meeting its goal — a tobacco-free society by the year 2000. (According to the Dec. 23 BUSINESSWEEK, cigarette sales dropped only 1.1 percent in 1985.)

Although a survey of 1,040 doctors reported in the December AMERICAN JOURNAL OF PUBLIC HEALTH ranked smoking cessation at the top of steps an individual can take to good health, Bigelow says only 20 percent of smokers report having been told to quit by their doctors. Rather, smokers most often quit after adverse health effects appear, "like closing the barn door after the horse is out," says Bigelow. Despite evidence that cessation even in middle age produces health benefits, the tobacco withdrawal syndrome — anxiety, irritability and lack of concentration — undermines good intentions. The most critical aspect, according to Bigelow, is the "constant craving" that can persist for months or even years after that last cigarette. Based on unfinished studies he has recently reviewed, Bigelow calls low-tar cigarettes used by concerned smokers "an illusory benefit being offered smokers," who compensate by inhaling deeper and taking bigger puffs.

More new studies give mixed reviews to other cessation aids and cigarette substitutes. A report in the Dec. 20 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION from the University of Minnesota in Minneapolis concludes that smokers should be advised to quit altogether rather than switch to a pipe or cigars. This recommendation is based on measurements of serum thiocyanate, a marker for inhaled tobacco smoke (SN: 12/3/84, p.360). The October CLINICAL PHARMACOLOGY AND THERAPEUTICS includes a report, from the Veterans Administration Medical Center and the University of California in Los Angeles, stating that the use of nicotine-containing skin patches significantly lowered cigarette craving compared with a placebo patch and avoided the possible side effects of nicotine gum. NIDA's Henningfield says his group is just starting evaluation of "smokeless cigarettes," currently being test-marketed in Texas as a product to eliminate some effects of smoking. The plastic tubes deliver nicotine vapor, not smoke or tar. But the results from nicotine research suggest such products would dull only one side of a double-edged sword.

The unresolved issue of dependency is made even more worrisome, several researchers told SCIENCE NEWS, by tobacco's availability, its low cost relative to illegal drugs and its social acceptability. "You can say nicotine is in the category of heroin and the stimulants," Henningfield notes, "but there are very few offices where you can shoot heroin."