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FACT SHEET **June 2009**

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Nicotine Increases Alcohol Craving

Smoking Tobacco Linked to Alcohol Relapse
People who smoke and try to quit drinking have a more difficult time not relapsing, because new scientific evidence indicates that nicotine may actually cause a craving for alcohol. If you combine this factor with another new study which indicates that nicotine addiction may be as powerful as an addiction to heroin, smokers who want to stop drinking face an extremely difficult battle indeed. Although many treatment programs and self-help support groups recommend addressing "one addiction at a time," treatment approaches that insist that clients give up all addictive substances simultaneously may be more effective, according to these new studies.

Alcohol-Nicotine Relationship
Led by Toronto's Dr. Dzung Anh Le, a study on rats by Canadian and U.S. scientists has found that nicotine use increases alcohol consumption, and the two addictions may work hand in hand.

The research relevant to humans who drink both excessively and moderately, said Dr. Le. It suggests that to quit drinking, a person might also have to give up smoking as well. "It has a lot of implications for treatment strategy," said Dr. Le, of the Centre for Addiction and Mental Health. "What we knew before is alcohol and tobacco are extensively co-abused. We wanted to find a biological basis for this co-dependency."

Dr. Ted Boadway of the Ontario Medical Association said although treating dual addictions is already a cornerstone of many therapies, anti-smoking strategies do not always emphasize curbing alcohol intake. Guidelines on stop-smoking approaches usually do not consider the effect alcohol may have on smokers. The study appears in the U.S. journal Alcoholism: Clinical and Experimental Research.

The Research
It is nicotine, the addictive ingredient in cigarettes, which leads to an increase in alcohol consumption, said Dr. Le and fellow researchers at the Indiana University School of Medicine. "Of the study's five experiments on rats, three confirmed researchers' suspicions that nicotine and alcohol "can act through the same rewarding system in the brain," said Dr. Le.

Both nicotine and alcohol lead to the release of dopamine, the "feel-good brain chemical," although the mechanism by which this occurs is not completely understood, Dr. Le said. "Repeated exposure to nicotine through smoking can enhance the pleasurable effects of alcohol, and there's probably some biological basis for this," although it's not completely understood.

The remaining two experiments in Dr. Le's study examined nicotinic receptor antagonists in the brain, and whether they could be altered to block the effects of nicotine and alcohol.

Highly Addictive
Meanwhile, the Royal College of Physicians in Britain released a report calling nicotine "a powerful addictive substance on a par with heroin and cocaine" which should be controlled like a drug or medicine.
The report said cigarettes are nicotine delivery products and said nicotine addiction should be recognized as a major medical and social problem. "It is time for nicotine to become a major health priority," Sir George Alberti, the president of the college, said.
The tobacco industry disputed the report's findings.
These new reports provide scientific evidence that those who try to quit drinking, but continue to smoke, face a more difficult problem than those who do not smoke, or who quit smoking and drinking simultaneously.

Other Cravings
Also this week, National Institute on Drug Abuse researchers released two studies that found that craving for nicotine appears to be linked to increased craving for illicit drugs among drug abusers who also smoke tobacco. The two studies, said NIDA Director Dr. Alan I. Leshner, "add very strong behavioral evidence to other research that suggests common characteristics and interactions between tobacco use and opiate and cocaine use. They also suggest that smoking cessation programs should be offered as part of other drug treatment programs."
In one of the studies, researchers found that the amount of cocaine and heroin use was directly related to the level of tobacco use. "The more cigarettes smoked, the more likely the person was to use illegal drugs," said Dominick Frosch, a doctoral student at San Diego State University.

Alcohol and Tobacco

Alcohol Alert From NIAAA
Extensive research supports the popular observation that "smokers drink and drinkers smoke." Moreover, the heaviest alcohol consumers are also the heaviest

consumers of tobacco.

Concurrent use of these drugs poses a significant public health threat. A survey of persons treated for alcoholism and other drug addictions revealed that 222 of 845 subjects had died over a 12-year period; one-third of these deaths were attributed to alcohol-related causes, and one-half were related to smoking (1). This *Alcohol Alert* explores the association between alcohol and tobacco use, possible mechanisms of their combined health effects, and some implications for alcoholism treatment.

The Co-Occurrence of Alcoholism and Smoking

Between 80 and 95 percent of alcoholics smoke cigarettes (2), a rate that is three times higher than among the population as a whole. Approximately 70 percent of alcoholics are *heavy* smokers (i.e., smoke more than one pack of cigarettes per day), compared with 10 percent of the general population (3). Drinking influences smoking more than smoking influences drinking. Nevertheless, smokers are 1.32 times as likely to consume alcohol as are nonsmokers (4). Most adult users of alcohol or tobacco first tried these drugs during their early teens (5). Among smoking alcoholics, the initiation of regular cigarette smoking typically precedes the onset of alcoholism by many years, although data are inconsistent (6). Adolescents who begin smoking are 3 times more likely to begin using alcohol (7), and smokers are 10 times more likely to develop alcoholism than are nonsmokers (6).

Why Are Alcohol and Tobacco Used Together?

Postulated mechanisms for the concurrent use of alcohol and tobacco fall into two broad, nonexclusive categories: Either drug may increase the desired (rewarding) effects of the other, or either may decrease the toxic or unpleasant (aversive) effects of the other. These interactions involve processes of reinforcement or tolerance, as described below. (A third possibility--that one drug may alter the metabolism of the other, thereby affecting its absorption, distribution, or elimination from the body--has not been convincingly established [8].)

Reinforcement.

Reinforcement refers to the physiological processes by which a behavior--such as consumption of a drug--becomes habitual. A key process in reinforcement for some drugs occurs when nerve cells release the chemical messenger dopamine into a small area of the brain called the nucleus accumbens following consumption of the drug (9). Nicotine is the primary ingredient of tobacco that triggers reinforcement. After reaching the brain, nicotine activates a group of proteins called nicotinic receptors. These proteins, located on the surface of certain brain cells, normally regulate a host of physiological functions, some of which may contribute to aspects of reinforcement. Ultimately, nicotine brings about the release of dopamine in the nucleus accumbens (5). Alcohol consumption also leads to dopamine release, although the mechanism by which alcohol produces this effect is incompletely understood (10,11).

Tolerance.

Tolerance is decreased sensitivity to a given effect of a drug such that increased doses are needed to achieve the same effect. Long-term administration of nicotine in animals can induce tolerance to some of alcohol's reinforcing effects, and chronic alcohol administration induces tolerance to some effects of nicotine (8). Such cross-tolerance might lead to increased consumption of both drugs in an attempt to regain former levels of reward. In addition, cross-tolerance can develop to the aversive effects of drugs. For example, smokers may reduce their tobacco intake when they begin to feel its aversive effects (e.g., increased heart rate, "nervousness"). Alcohol's sedating effects may mitigate these effects of nicotine, facilitating continued tobacco use (12). Conversely, nicotine's stimulating effects can mitigate alcohol-induced loss of mental alertness (8).

Animal studies provide support for these interactions. For example, alcohol appears to induce loss of physical coordination in mice by inhibiting nicotinic receptors in the cerebellum, a part of the brain that is active in coordinating movement and balance. Administration of nicotine appears to remove this inhibition and restore coordination (13,14). In addition, alcohol interferes with the normal functioning of the chemical messenger vasopressin, which may play a role in memory processes. Vasopressin is also associated with the development of tolerance to alcohol (15). Nicotine helps normalize vasopressin function in the brain, reducing alcohol-induced impairment of memory and other intellectual abilities (11).

What Is the Risk of Cancer From Alcohol and Tobacco?

Smoking and excessive alcohol use are risk factors for cardiovascular and lung diseases and for some forms of cancer. The risks of cancer of the mouth, throat, or esophagus for the smoking drinker are more than the sum of the risks posed by these drugs individually (2). For example, compared with the risk for nonsmoking nondrinkers, the approximate relative risks for developing mouth and throat cancer are 7 times greater for those who use tobacco, 6 times greater for those who use alcohol, and 38 times greater for those who use both tobacco and alcohol (16).

How Do Alcohol and Tobacco Increase Cancer Risk?

Approximately 4,000 chemical substances are generated by the chemical reactions that occur in the intense heat of a burning cigarette (17). A group of these chemicals, collectively known as tar, is carried into the lungs on inhaled smoke. The bloodstream then distributes the components of tar throughout the body. Certain enzymes found mainly in the liver (i.e., microsomal enzymes) convert some ingredients of tar into chemicals that can cause cancer. Long-term alcohol consumption can activate some such microsomal enzymes, greatly increasing their activity and contributing to smoking-related cancers (18,19).

Microsomal enzymes are found not only in the liver but also in the lungs and digestive tract, which are major portals of entry for tobacco smoke. The esophagus may

be particularly susceptible, because it lacks an efficient mechanism for removing toxic substances produced by activated microsomal enzymes (20). Consistent with these observations, alcohol has been shown to promote esophageal tumors in laboratory animals exposed simultaneously to specific components of tar (18,19). Finally, alcoholics frequently exhibit deficiencies of zinc and vitamin A, substances that confer some protection against cancer (20).

Addictions Treatment for Smoking Alcoholics

Until recently, alcoholism treatment professionals have generally not addressed the issue of smoking cessation, largely because of the belief that the added stress of quitting smoking would jeopardize an alcoholic's recovery (21).

Research has not confirmed this belief. One study evaluated the progress of residents in an alcoholism treatment facility who were concurrently undergoing a standard smoking cessation program (i.e., experimental group) (6). A comparison group of smoking alcoholics participated in the same alcoholism program but without undergoing the smoking cessation program. One year after treatment, results indicated that the smoking cessation program had no effect on abstinence from alcohol or other drugs. In addition, 12 percent of the subjects in the experimental group, but none of the subjects in the comparison group, had stopped smoking.

Some data suggest that alcoholism recovery may facilitate nicotine abstinence. In one study, patients participating in concurrent treatment for nicotine addiction during residential treatment for alcohol and other drug abuse achieved at least a temporary reduction in smoking and an increased motivation to quit smoking (22). Similarly, persons who achieve abstinence from alcohol without formal treatment often stop smoking at the same time (6,23).

Following the lead of other health facilities, many addictions treatment facilities are becoming smoke-free, providing a "natural experiment" on the effectiveness of dual recovery programs. Initial evaluations suggest that no -smoking policies are feasible in this setting (24). However, no outcome studies have been performed, and additional research is needed.

Problems encountered in smoke-free alcoholism treatment programs include surreptitious smoking by patients as well as by staff. Further, researchers have suggested modifying smoking cessation programs to conform with the structure and language of concurrent alcoholism programs (e.g., use of a 12-step approach) (2). Nicotine patch therapy for smoking alcoholics may require higher doses of nicotine than are usually applied, because of alcohol-induced tolerance to some of nicotine's effects (25,26). Smoking alcoholics with a history of depressive disorders are generally less successful at smoking cessation than are subjects without such a history (27). Smoking may diminish the chances of recurring depression in some people, and a major depressive episode may follow smoking cessation in these subjects (28). An additional clinical consideration is that activation of microsomal enzymes by alcohol and tobacco tar may reduce the effectiveness of antidepressant medications (17). Therefore, medication levels should be carefully monitored in patients undergoing treatment for depression and addiction to alcohol and tobacco (5).

Alcohol and Tobacco--A Commentary by NIAAA Director Enoch Gordis, M.D.

Alcohol and tobacco are frequently used together, may share certain brain pathways underlying dependence, and because of their numerous social and health-related consequences, are a continuing source of national public policy debate.

Many alcoholism treatment professionals have not actively pursued smoking cessation among their patients based on the belief that the stress of quitting smoking while undergoing alcoholism treatment might cause relapse. As a physician who has seen the ravages caused by both alcoholism and smoking, I am pleased that we now have research evidence showing that both can be treated simultaneously without endangering alcoholism recovery. As basic science learns more about how alcohol and nicotine act singly and together within the brain, new treatments for alcohol and nicotine dependence will follow. Finally, society has attempted to minimize the consequences of using both alcohol and tobacco through public policy actions, including health warning labels, restrictions on advertising, and age restrictions on use. Unlike tobacco, however, moderate use of alcohol has certain health benefits. The implications of this are discussed in *Alcohol Alert* No. 16, "Moderate Drinking," which may be found on NIAAA's Web site at www.niaaa.nih.gov.

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Alcohol and Nicotine

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