Alcohol, a Carcinogen?

The Editor interviews:
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Editor: What is the etiological relationship between cancer and alcohol?

Dr. Seixas: The precise etiological relationship has not been entirely determined. Although no experimental evidence directly proves that alcohol is a carcinogen, substantial epidemiological data correlate certain cancers with chronic alcoholism.

Editor: How is chronic alcoholism defined?

Dr. Seixas: The World Health Organization defines chronic alcoholism as the psychological, physical and physiological dependence on alcohol. Physiological addiction is characterized by specific withdrawal syndromes.

Editor: What is the risk of cancer for heavy drinkers?

Dr. Seixas: The figure cannot be given exactly; percentages vary according to the cancer site and the investigator. (Table 1.) A study by Rothman and Keller indicated that men who drank more than three ounces of whiskey and smoked 40 or more cigarettes daily were 15 times more susceptible to oral cancer than the general population. They concluded that smoking and alcohol consumption together accounted for 75 percent of oral cancer in men. (Table 2.) Wynder found that the risk of esophageal cancer for a heavy whiskey drinker is about 25 times that for a nondrinker, when tobacco consumption is held constant. Although it is rare to find a group of heavy drinkers who do not also smoke, Wynder has suggested that alcoholism without smoking doesn’t increase the risk of oral cancer.

Editor: Do variations in drinking habits affect the risk of cancer?
TABLE 1
THE RELATIONSHIP BETWEEN CANCER AT VARIOUS SITES AND THE USE OF ALCOHOL AND TOBACCO*

| Sites              | Number of Cases | Relationship with use of alcohol | Relationship with use of tobacco | Sex Ratio (M:F) |
|--------------------|----------------|---------------------------------|---------------------------------|-----------------|
| Hypopharynx        | 4,225          | very strong                     | very strong                     | 28.0            |
| Larynx             | 5,524          | very strong                     | very strong                     | 27.4            |
| Esophagus          | 5,007          | very strong                     | strong                          | 16.6            |
| Lung               | 4,616          | strong                          | very strong                     | 11.8            |
| Oropharynx         | 3,216          | strong                          | very strong                     | 11.6            |
| Tongue             | 4,856          | very strong                     | strong                          | 9.3             |
| Oral cavity (other sites) | 4,145      | strong                          | very strong                     | 8.6             |
| Lips               | 3,609          | strong                          | strong                          | 8.1             |
| Bladder and other urinary organs | 962         |                                 | strong                          | 2.6             |

*Source: Flamant, R., et al.: Differences in sex ratio according to cancer site and possible relationship with use of tobacco and alcohol; review of 65,000 cases. J. Nat. Cancer Inst. 32: 1309-1316, 1964.

TABLE 2
RELATIVE RISK OF ORAL CANCER ACCORDING TO LEVEL OF EXPOSURE TO ALCOHOL AND SMOKING*

| Ounces of Alcohol Per Day | Cigarette Equivalents Per Day |
|---------------------------|-------------------------------|
|                           | 0 | Less than 20 | 20-39 | 40 or More |
| No alcohol                | 1.00 | 1.52 | 1.43 | 2.43 |
| Less than 0.4 oz.         | 1.40 | 1.67 | 3.18 | 3.25 |
| 0.4 - 1.5 oz.             | 1.60 | 4.36 | 4.46 | 8.21 |
| More than 1.5 oz.         | 2.33 | 4.13 | 9.59 | 15.50 |

*Source: Rothman, K., and Keller, A.: The effect of joint exposure to alcohol and tobacco on risk of cancer of mouth and pharynx. J. Chron. Dis. 25: 711-716, 1972. Risk is expressed relative to a risk of 1.00 for persons who neither smoked nor drank.

Dr. Seixas: Yes, in fairly predictable ways. Generally, the more alcohol consumed, the greater is the chance of developing certain cancers. Wynder, Bross and Feldman found that heavy drinkers were 10 times more susceptible to oral cancer than moderate drinkers when all other factors were equal. Some investigators also found that consumption of whiskey rather than wine or beer was more often linked to the development of cancer, perhaps because of a higher alcohol content.
The duration of alcoholism seems to be another important factor. In a continuing study of 3,000 alcoholics, Kissin discovered eight cases of head and neck cancer in the following locations: floor of mouth (3), tonsils (1), parotid (1), soft palate (1), base of the tongue (1) and lymphoid gland (1). This compares with an expected incidence of one in 3,000. No cancers were found among 3,000 matched nonalcoholic controls. Importantly, in the alcoholic group, the duration of drinking and smoking was generally longer in those who developed cancer than in those who did not, even when total consumption was not significantly different.

Editor:  
_Then the evidence suggests that alcoholics are more prone to head and neck cancer than nondrinkers?_

Dr. Seixas:  
Yes. In a classic epidemiologic study by Wynder and associates, alcohol consumption was identified as one of the major factors in the development of cancer of the oral cavity and larynx. The laryngeal tumors were more likely to be extrinsic than intrinsic in type. Supporting data are provided by Keller’s findings that cancer of the head and neck is associated with cirrhosis of the liver, a secondary manifestation of alcoholism.

Editor:  
_Are other cancers related to alcoholism?_

Dr. Seixas:  
There is considerable evidence linking alcoholism to cancer of the esophagus—at least in western countries. Horie et al. induced esophageal cancer experimentally by injecting mice with the carcinogen, benzo (a) pyrene 4-nitroquinoline-1-oxide diluted in ethanol, while oral administration of the carcinogen dissolved in oil rather than alcohol did not produce tumors. In clinical studies of 101 patients with esophageal cancer, Mosbeck found that 65 percent were alcoholics; Lynch reported an alcoholism rate of 70 percent among his esophageal cancer patients. Many other studies also confirm this association. However, according to some investigators, alcohol alone is not related etiologically to esophageal cancer. For example, alcoholism is rare in Iran where the incidence of esophageal cancer is the highest in the world.

Research has also been done on the relationship between alcoholism and cancer of the skin, lung, stomach and pancreas. But, the findings are not as definitive as they are for oral, esophageal or liver cancer; further evaluation is needed.

Editor:  
_Could cancer be caused by the secondary effects of alcoholism?_

Dr. Seixas:  
Probably. There is a good deal of data implicating cirrhosis of the liver in the pathogenesis of hepatoma; Davidson found that cirrhosis is present in about 70 percent of patients with primary liver cancer. Surprisingly, there is a higher incidence of hepatoma in patients with mild or healed alcoholic cirrhosis than in those with severe, acute disease. Cessation of drinking in patients with well-
established cirrhosis does not prevent hepatoma. In addition, alcohol-related malnutrition and/or vitamin deficiencies have been described as a causative factor in several studies of esophageal, head and neck cancer.

Editor: What is the pathogenic mechanism by which alcohol may contribute to the development of cancer?

Dr. Seixas: The exact mechanism is not known; however several theories have been formulated. It is hypothesized that alcohol may enhance the effect of environmental carcinogens such as those identified in cigarette tars, perhaps by increasing their diffusion into tissues. Some investigators feel that alcohol could interfere with normal salivary flow, prolonging exposure to tobacco tars. In addition, a number of substances such as aromatics, alkaloids and polycyclic hydrocarbons are present in alcoholic beverages and could possibly be carcinogenic. Aflatoxin in Japanese rice wine is an example of a proven carcinogen in alcohol. And, finally, alcohol may predispose the body tissues to carcinogenesis directly.

Editor: How many cancers do you estimate could be prevented if no one drank alcohol?

Dr. Seixas: In the United States virtually all hepatomas associated with alcoholic cirrhosis could be prevented if the patient stopped drinking before developing cirrhosis. The number of esophageal and oral cancers that could be eliminated by abstinence from drinking and smoking is also substantial. In a 1961 study, Wynder estimated that the incidence of esophageal cancer in the United States would be reduced by at least 80 percent if no one drank or smoked.

Editor: What is actually being done to make this reduction a reality?

Dr. Seixas: Epidemiological research and long-term prospective studies of alcohol consumption and cancer are now under way. The first large-scale epidemiologic study was begun by the American Cancer Society in 1959. One million Americans are being followed to determine the correlation between alcohol consumption and the development of cancer. Another large prospective study of 265,118 men and women aged 40 years and over has also been carried out by Hirayama in Japan. Eventually, these projects may yield significant data.

Educational efforts must be increased so that physicians can more easily recognize and effectively treat alcoholics. The National Council on Alcoholism has developed a helpful pamphlet, Criteria for the Diagnosis of Alcoholism, and our 170 member organizations throughout the country provide information and referral services for alcoholics and their families.

Editor: Thank you, Dr. Seixas.