

Epidemiology of Alcohol and Cancer¹

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Abstract

There is still insufficient knowledge of the distribution of drinking habits in human populations, and more descriptive surveys are needed.

Both prospective and retrospective epidemiological studies indicate that alcohol consumption is a cancer hazard. Prospective studies on excessive drinkers have shown an increased risk for cancer of the mouth, pharynx, larynx, esophagus, liver, and lung. Retrospective studies have confirmed this excess risk. For cancers of the buccal cavity, pharynx, larynx, and esophagus, the effect of drinking has been shown to be associated with the effect of smoking. In the case of esophageal cancer, these two effects are independent, and the observations made are consistent with a multiplicative model. Primary liver cancer is also associated with alcohol consumption, probably by a less direct action; the importance of the impact of alcohol on primary liver cancer is probably underestimated.

Animal experiments have not shown that ethanol alone has a carcinogenic effect, and the mechanisms by which alcoholic beverages act on humans remain unknown.

The proportion of cancer cases at sites known to be associated with alcohol consumption is approximately 8% in most population groups in the United States. This indicates that a sizeable proportion of cancers is potentially preventable if appropriate action is taken.

Epidemiology of Alcohol Consumption

The most recent figures available on alcohol consumption per capita are for 1972 (5), and they show that in almost all countries in the world average consumption is increasing. The only exception to this is France, where figures are slowly but steadily decreasing. France nevertheless maintains the leadership as to average amount of alcohol consumed by an individual.

These consumption figures, however, are based on the sales of alcoholic beverages referred to the adult population in each country. It is well known that even though such figures provide an acceptable estimate of overall consumption, they are inadequate in describing the distribution of alcohol consumption in a human population. That distribution does not follow a "normal" pattern when consumption classes are shown on an arithmetic scale; to bring it closer to a normal distribution, the representation must be done on a logarithmic scale of average consumption, and the distribution can then be expressed by an equation from which one can derive the proportion of individuals who drink more than a given threshold. This proportion is somehow related to the overall total consumption in a given country, and Ledermann (12) has expressed this relationship in an equation. Whether this relationship is as simple

as Ledermann thought is presently a matter of controversy (2, 3) and will not be discussed here.

What is undeniable, however, is the need for more surveys providing a good description of drinking habits in human populations. We need to know how people consume alcohol in terms of average daily consumption by sex, age, social class, type of drink, rhythm of drinking, and possibly by more parameters. Such a detailed description can only be obtained by direct measurement within well-designed surveys. There are surprisingly few surveys of this kind, and very little is known about the way people consume their alcohol throughout the world. This is probably the reason why little is known of the risks of developing various diseases in relation to alcohol consumption. There is a great need for more surveys describing alcohol consumption habits which could provide denominators for epidemiological studies on the various diseases that are known or suspected to be influenced by alcohol consumption.

As far as cancer is concerned, one known feature is of great importance, that is, the relationship between drinking and smoking habits. There are more heavy smokers among drinkers and fewer smokers among abstainers. This has been shown in various circumstances; Wynder and Bross (26) showed this in an American population, and the same was found in a more recent survey in Brittany (25).

One of the very first studies on the relationship between cancer and alcohol consumption was undertaken in France by Schwartz *et al.* (19). These authors recorded the average daily alcohol consumption in a large range of cancer patients and calculated the average consumption for each type of cancer. The result was a scale showing that these averages were highest among patients with cancer of the hypopharynx, esophagus, tongue, larynx, oropharynx, and mouth. These findings were later confirmed by a large number of studies undertaken in various human groups.

Prospective Studies of Excessive Drinkers

In the first group of studies, people known or reputed to be alcoholics were assembled in cohorts, the fate of which was then compared with that of the general population. These were either patients who had been hospitalized at some time for a disease related to excessive alcohol consumption, or more simply as alcohol misusers, for example, people having committed an offence while under the influence of alcohol (7, 15, 16, 18).

All these studies showed similar results; the people in such cohorts of drinkers always showed an excess of cancer of the mouth, pharynx, larynx, esophagus, liver, and lung (21).

Reciprocally, studies of the same design relating to human groups known to be abstainers, such as Seventh-Day Adventists or Mormons, showed results of the same significance; all the cancers enumerated above being less frequent than in a normal population (4, 13, 14, 29).

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These prospective studies have a great advantage in common which is to provide data on various causes of death such as cirrhosis of the liver, accidents, etc., as well as for cancer.

They also have some disadvantages in common. They do not provide information on the amount of alcohol intake and thus do not permit the study of a gradient in the risk of disease in relation to individual consumption. Also, they do not provide an indication of other parameters of interest such as smoking, for example, and it is commonly accepted that the excess of cancer of the lung observed among drinkers is related to their smoking rather than to their drinking.

One recent study undertaken in Denmark by Jensen (10) showed the potentialities of prospective studies for testing a working hypothesis.

In 1974, Breslow and Enstrom (1) studying the correlation between various cancers and the reported average consumption of alcohol per capita, described a correlation between beer consumption and cancer of the rectum. This was found for the states within the United States as well as for European countries. This finding was indeed of great concern to people with a large consumption of beer.

To study whether this relationship could be confirmed by an appropriate epidemiological study, Jensen reviewed the fate of Danish brewery workers who had been affiliated to the Brewery Workers Union from 1939 to 1963. After elimination of duplicates and other appropriate adjustments, he had a large cohort of 14,313 people who had been employed at some time in their lives in the manufacture of beer. These people are known to have received an average of 6 pints of free beer per day, that is a little more than 2 litres per day, a consumption estimated to be 4 times higher than that of the male general population in Denmark.

Thanks to the detailed mortality and cancer morbidity registries which exist in that country cancer mortality and morbidity experience for those brewery workers could be examined and compared to that observed in the general Danish population.

When Jensen examined total mortality, he found an excess total mortality among brewery workers and an excess of deaths from gastrointestinal tract diseases and cancer. When looking at various types of cancer, he found that this excess was mainly for cancer of the esophagus and larynx and, to a lesser extent, cancer of the liver.

When looking at morbidity data, Jensen found an excess for the same cancer sites as was found for mortality data. He was further able to distinguish, among workers affiliated to the Union, those who had worked in the production of mineral and soda water as opposed to the larger number involved in the brewery work itself. He showed that the latter only had an excess of cancers while the small group working in the production of mineral and soda water did not. In view of the finding of Breslow and Enstrom of a correlation between beer consumption and rectal cancer, Jensen looked with great care at risks for cancers of the colon and rectum; there was no excess risk for either.

A study of the same kind was undertaken by Dean *et al.*;² the data of that study showed some different results insofar as there were observed 32 cancers of the rectum versus 18 that were expected.²

² G. Dean, P. MacLennan, H. McLoughlin, and E. Shelly. The causes of death of blue-collar workers at a Dublin Brewery, submitted for publication.

Retrospective Case-Control Studies

These studies usually refer to one or more cancer sites. Cancer of the buccal cavity and pharynx have been investigated by several authors. Wynder *et al.* (27) clearly showed the role of alcohol, and Rothman and Keller (17) further demonstrated a combined effect of alcohol and tobacco. Their data were consistent with an additive effect of the 2 parameters.

Cancer of the larynx is also related to alcohol consumption, but Wynder *et al.* (28) found that this effect was mainly among smokers, while among nonsmokers there was no apparent effect of alcohol drinking. Cancer of the larynx is a frequent disease in southwest Europe; the highest mortality figures are observed in France, Italy, and Spain which also happen to be countries with very high average wine consumption. This is now being investigated (9).

Cancer of the esophagus has been known to be associated with heavy drinking and heavy smoking. Wynder (26), in his New York study, was able to show that each of these 2 factors plays a role independently of the other.

More recent data have confirmed this in Europe. While most European countries have rather low mortality rates for esophageal cancer, France is a remarkable exception, and within that country, the highest rates have been observed in the west coast provinces of Brittany and Normandy. Mortality from alcoholism and cirrhosis of the liver was found to be particularly high in the same provinces (20), and this finding justified the extensive studies undertaken in Ille-et-Vilaine, one of the départements in Brittany.

In this study, relative risks were calculated for various levels of alcohol consumption after adjustment for tobacco consumption and also for various levels of tobacco consumption after adjustment for alcohol intake. The logarithm of the relative risk in each case was found to be a linear function of daily alcohol consumption and daily tobacco consumption. When alcohol and tobacco intake were considered together, the risks observed were consistent with a multiplicative model (25). First results of a similar study undertaken in Calvados showed a similar relationship for alcohol consumption and also provided some evidence that the risk would be higher for certain alcoholic beverages heavily consumed in the département, namely apple cider and its distillates.³

Liver cancer is another cancer associated with alcohol consumption, but the mechanisms are probably different since the liver is not in direct contact with alcoholic beverages when they are ingested. The problem of primary liver cancer is closely associated with that of cirrhosis of the liver. There are a large number of publications showing that 60 to 90% of primary liver cancers are associated with cirrhosis of the liver, and in many countries of the western world, cirrhosis is known to be associated with excessive alcohol consumption. The relation between primary liver cancer and cirrhosis can be expressed in a reciprocal way by establishing among all cases of cirrhosis the percentage where there is also primary liver cancer; this proportion varies from 5 to 30% (22).

Primary liver cancer is generally considered to be a rare disease in the western world. There is one observation, however, that incidence of this disease might reach a sizable level:

³ A. J. Tuyns, G. Péquignot, and J. S. Abbatucci. Esophageal Cancer and Alcohol Consumption. Importance of type of beverage, submitted for publication.

Table 1

Age-adjusted annual incidence rates for selected cancer sites in various population groups in the United States

Source: A. Tuyns. *Alcohol and Cancer. Paper prepared for National Institute on Alcohol Abuse and Alcoholism under Contract HSM 42-73-116, 1977.*

Place	Population	Tongue	Mouth	Oropharynx	Hypopharynx	Esophagus	Liver	Larynx	Total for the 7 cancer sites	Proportion of all cancers (%)
California										
Alameda	White	3.0	3.7	2.2	1.1	3.6	2.2	7.9	23.70	8.5
	Black	2.2	4.1	2.2	1.5	13.2	4.3	12.9	40.40	12.3
Bay Area	White	3.2	4.2	2.6	1.5	4.0	2.8	7.5	25.80	8.6
	Black	2.1	4.8	3.3	1.5	15.2	4.2	11.8	42.90	12.5
Connecticut		2.8	4.3	2.1	1.5	5.7	2.0	7.8	26.20	9.2
Iowa		1.4	2.6	1.1	1.2	3.0	1.6	5.8	16.70	6.7
Detroit	White	2.7	3.3	2.0	1.2	4.0	2.6	7.5	23.30	8.7
	Black	3.3	3.3	2.1	1.1	14.1	4.5	7.7	36.10	11.3
New Mexico	Spanish	0.4	0.7	0.4	0.2	2.2	3.0	2.7	9.60	6.1
	Other white	2.2	2.8	1.4	0.3	3.0	3.1	5.8	18.60	6.7
New York State		2.2	3.2	1.3	0.8	4.5	1.9	5.9	19.80	8.0
Puerto Rico		7.5	7.8	4.3	4.4	14.8	3.3	6.4	48.50	27.9
Utah		2.1	2.5	0.9	0.4	1.8	0.9	4.4	13.00	6.1

in Geneva, incidence was found to be 10/100,000, a figure much higher than anticipated in a European population (23). Geneva benefits from a remarkably high proportion of autopsies, and this might have influenced the rate observed. One may wonder, however, whether this very high incidence is an exceptional feature or whether in other countries with a lower rate of autopsies, the figures for primary liver cancer are underestimated.

Mechanisms of Action

There is no doubt that the consumption of alcohol entails an increased risk for cancer of the buccal cavity, pharynx, larynx, esophagus, and liver. The mechanisms by which this occurs are not yet known. There is no evidence that pure ethanol *per se* should be carcinogenic, and most authors believe that alcoholic beverages are carcinogenic rather by some carcinogens included in the beverages than by ethanol itself.

Several groups of chemicals have been suspected to be responsible. Gibel *et al.* (6) believe that fusel oil, which is often present in many strong alcoholic beverages, is carcinogenic.

On the other hand, Japanese authors Horie *et al.* (8), and Kuratsune *et al.* (11) have been able to show that benzo(a)pyrene can penetrate esophageal mucosa when diluted in ethanol. This is a mechanism that seems to resemble what might happen in human usage. Walker *et al.*⁴ have examined the possibility that nitrosamines may be present in beverages. They were able to demonstrate the presence of a certain number of these substances in samples collected from high-risk areas; the quantities found, however, were minute, and one may doubt whether these explain an excess risk.

Size of Problem and Possibility of Prevention

The number of deaths from cancers known to be related to

⁴ E. A. Walker, M. Castagnaro, L. Garren, and G. Toussaint. Determination of volatile nitrosamines in alcohol drinks and their relationship to incidence of esophageal cancer, submitted for publication.

alcohol consumption represents an appreciable proportion of total cancer mortality in the United States as can be seen in Table 1. This proportion varies from country to country, and in France, it reaches 20% in males for 1968 to 1970 (22).

There is no doubt that a policy aiming at encouraging people to reduce their alcohol and tobacco intake would result in a considerable decrease in incidence of the various cancers enumerated above. How this can be achieved is a complicated matter since it might be very difficult to make people understand that a danger exists for what they consider to be reasonable alcohol intake. In this respect, it seems that some of the findings in the Ille-et-Vilaine studies may help health educators. Based on good scientific ground, some of the graphs available are particularly suggestive and easy to understand. One argument sometimes used in France to encourage people to drink and smoke less is that if French males in Brittany smoked and drank as little as do their spouses, they would probably enjoy the same esophageal cancer rate, which is 20 times lower than their own (25).

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