A study of cases of cancer of the mouth and pharynx showed that such cancers are associated with cirrhosis of the liver, and independently with heavy alcohol consumption and smoking. These findings occur much less frequently among Jews. The authors conclude that there is a significant relationship between heavy alcohol consumption and smoking, and cancer of the mouth and pharynx.

THE ASSOCIATION OF ALCOHOL AND TOBACCO WITH CANCER OF THE MOUTH AND PHARYNX

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THE association of smoking with cancer of the mouth and pharynx has been demonstrated by a number of studies.[1-9] Vincent and Marchetta[8] found, in a series of 106 cases of oral and pharyngeal cancer, an association with the use of both tobacco and alcohol. Wynder, Bross and Feldman[5] reported that, for a series of 659 cases, cancer of the mouth and pharynx was apparently associated independently with both alcohol consumption and smoking.

Keller[10] found, in a series of 2,177 cases of lip, oral, and pharyngeal cancers, a strong association of cancer of the floor of the mouth and liver cirrhosis. No association was found between any of these cancers and syphilis, diabetes mellitus, or arteriosclerosis; an association of tongue cancer and alcoholism was rejected. The present study was undertaken to investigate further the relation of cancer of the mouth and pharynx to the use of tobacco and alcohol, and to liver cirrhosis, syphilis, and diabetes mellitus.

Materials and Methods

The study was limited to the three New York City Veterans Administration hospitals in Brooklyn, Manhattan, and the Bronx, each of which has more than 1,000 beds.

A case was a male with histologically confirmed squamous cell carcinoma of the tongue, floor of mouth, uvula and soft palate, mesopharynx, hypopharynx, other parts of the mouth, and multiple sites. All carcinomas corresponded to international rubrics 141, 143, 144, 145, and 147; and they were so entered into the cancer registers of each hospital for the period 1953-1963. The multiple sites comprised malignant neoplasms of the mouth and pharynx for which a most probable primary site could not be determined. The other parts of mouth included the alveolar ridge, buccal mucosa, hard palate, retromolar pad, and the gingiva. The anatomical site for each malignancy was ascertained by the careful review of entries in clinical records by the head and neck tumor boards, as well as the attending physicians. For each case, the control was the next male admission (determined by accession number) to the same hospital, who was in the same five-year age group.

Complete clinical records were reviewed for the 598 cases and the 598

age-matched controls in the study sample. All data were recorded on standard forms. These data included age at admission, pertinent histological findings, tobacco use, alcohol consumption, religious preference, occupation, and the diagnoses of liver cirrhosis, syphilis, and diabetes mellitus. The data were coded and entered on punch cards for analysis.

The proportion of deaths, and therefore of autopsies, was higher in the cases than in the controls. In order to avoid bias resulting from this difference, diagnoses of liver cirrhosis made only at autopsy were excluded from consideration. There were no diagnoses of syphilis or diabetes mellitus which were made only at autopsy.

Clinical records provided open-end entries on smoking and drinking histories which were routinely elicited by the admitting physicians. Cigarette equivalents for tobacco, and alcohol equivalents for drinking, were used in the analysis. From the 598 pairs matched on age, 134 pairs were found to match on tobacco equivalents and 154 pairs on alcohol equivalents. The alcohol and cigarette equivalent pairs were analyzed to determine whether tobacco and alcohol were independently associated with these cancers.

The matched chi-square test was used to determine the statistical significance of the differences found between cases and controls.[11]

Results

The age distribution of both cases and controls is: 30 to 39 years, 2.3 per cent; 40 to 49 years, 15.9 per cent; 50 to 59 years, 28.6 per cent; 60 to 69 years, 40.5 per cent; 70 to 79 years, 11.2 per cent; and 80 years and over, 1.5 per cent. The median age is 60 years.

The proportion of cases with clinically diagnosed liver cirrhosis is 19 per cent as compared with only 9 per cent of the controls (Table 1). This difference is significant at the 0.001 per cent level. A significant excess of liver cirrhosis among the cases is found for each of the individual sites except tongue and other parts of mouth.

Daily alcohol consumption is shown in Table 2. Among the cases, 43 per cent are heavy drinkers (1.6 ounces of alcohol or more per day) as compared

Table 1—Proportion with Clinically Diagnosed Liver Cirrhosis Among Cases of Cancer of Mouth and Pharynx and Age-Matched Controls by Site, Veterans Administration Hospitals, New York City

Site	Number	Liver Cirrhosis			
		Cases		Controls	
		No.	%	No.	%
Floor of mouth	160	41	25.6[x]	16	10.0[x]
Uvula and soft palate	20	7	35.0[y]	—	—[y]
Mesopharynx	59	9	15.3[z]	3	5.1[z]
Hypopharynx	36	7	19.4[z]	2	5.6[z]
Tongue	87	11	12.6	11	12.6
Other parts of mouth	46	6	13.0	4	8.7
Multiple sites	190	33	17.4[z]	19	10.0[z]
Total	598	114	19.1[x]	55	9.2[x]

x—P <0.00001
y—P <0.01
z—P <0.05

Table 2—Alcohol Consumption by Cases of Cancer of the Mouth and Pharynx and Age-Matched Controls, Veterans Administration Hospitals, New York City

Alcohol per Day (oz)*	Cases		Controls	
	No.	%	No.	%
None	53	8.9	121	20.2
<0.4	101	16.9	167	27.9
0.4-1.5	132	22.1	114	19.1
1.6+	258	43.1[x]	120	20.1[x]
Not stated	54	9.0	76	12.7
Total	598	100.0	598	100.0

* 0.4 oz=1 oz whiskey=4 oz wine=8 oz beer.
x—P <0.00001

with only 20 per cent of the controls. This difference is significant at the 0.001 per cent level. The excess of heavy drinking among the cases is significant for floor of mouth, mesopharynx, tongue, and multiple sites (Table 3). Mixed drinking is most common, and whiskey and beer are more commonly consumed than wine (Table 4).

Daily use of tobacco is shown in Table 5. Among the cases, 25 per cent are heavy smokers (40 cigarette equivalents or more per day) as compared with only 12 per cent of the controls. This difference is significant at the 0.001 per cent level. The excess of heavy smoking among the cases is significant for floor of mouth, tongue, and multiple sites (Table 6). "Cigarettes only" is the most common form of smoking, and the difference between cases and controls in the proportion smoking only cigarettes is significant at the 0.001 per cent level (Table 7).

Religious preference is shown in Table 8. Only 4 per cent of the cases are Jews as compared with 16 per cent of the controls. This difference is sig-

Table 3—Heavy Drinking* Among Cases of Cancer of Mouth and Pharynx and Age-Matched Controls by Site, Veterans Administration Hospitals, New York City

Site	Number	Cases		Controls	
		No.	%	No.	%
Floor of mouth	160	79	49.4[x]	32	20.0[x]
Uvula and soft palate	20	7	35.0	3	15.0
Mesopharynx	59	25	42.4[y]	11	18.6[y]
Hypopharynx	36	12	33.3	10	27.8
Tongue	87	37	42.5[y]	15	17.2[y]
Other parts of mouth	46	11	23.9	8	17.4
Multiple sites	190	87	45.8[x]	41	21.6[x]
Total	598	258	43.1[x]	120	20.1[x]

* 1.6+ oz alcohol per day (4+ oz whiskey, 16+ oz wine, 32+ oz beer).
x—P <0.00001
y—P <0.01

Table 4—Type of Drinking by Cases of Cancer of the Mouth and Pharynx and Age-Matched Controls, Veterans Administration Hospitals, New York City

Type of Drinking	Cases		Controls	
	No.	%	No.	%
None	53	8.9	121	20.2
Wine only	20	3.3	18	3.0
Beer only	93	15.5	82	13.7
Whiskey only	105	17.6	73	12.2
Mixed	299	50.0	251	42.0
Not stated	28	4.7	53	8.9
Total	598	100.0	598	100.0

Table 5—Use of Tobacco by Cases of Cancer of the Mouth and Pharynx and Age-Matched Controls, Veterans Administration Hospitals, New York City

Cigarette Equivalents per Day*	Cases		Controls	
	No.	%	No.	%
None	27	4.5	90	15.1
<20	70	11.7	100	16.7
20-39	264	44.1	213	35.6
40+	150	25.1[x]	72	12.0[x]
Not stated	87	14.6	123	20.6
Total	598	100.0	598	100.0

* 1 cigarette = ½ pipeful = ¼ cigar.
x—P <0.00001

Table 6—Heavy Smoking* Among Cases of Cancer of Mouth and Pharynx and Age-Matched Controls by Site, Veterans Administration Hospitals, New York City

Site	Number	Cases		Controls	
		No.	%	No.	%
Floor of mouth	160	47	29.4[y]	18	11.3[y]
Uvula and soft palate	20	4	20.0	4	20.0
Mesopharynx	59	15	25.4	8	13.6
Hypopharynx	36	6	16.7	7	19.4
Tongue	87	23	26.4[y]	9	10.3[y]
Other parts of mouth	46	12	26.1	9	19.6
Multiple sites	190	43	22.6[y]	17	8.9[y]
Total	598	150	25.1[x]	72	12.0[x]

* 40+ cigarettes or equivalents per day.
x—P <0.00001
y—P <0.01

Table 7—Type of Smoking by Cases of Cancer of the Mouth and Pharynx and Age-Matched Controls, Veterans Administration Hospitals, New York City

Type of Smoking	Cases		Controls	
	No.	%	No.	%
None	27	4.5	90	15.1
Cigarettes only	405	67.7[x]	329	55.0[x]
Cigars only	50	8.4	43	7.2
Pipes only	26	4.3	16	2.7
Mixed	61	10.2	76	12.7
Not stated	29	4.9	44	7.3
Total	598	100.0	598	100.0

x—P <0.00001

nificant at the 0.001 per cent level. On the other hand, 60 per cent of the cases are Catholics as compared with 50 per cent of the controls; the difference is significant at the 0.1 per cent level.

Alcohol consumption among the controls by religious preference is shown in Table 9. Protestants and Catholics consume similar quantities of alcohol, while Jews consume much less. The difference between the Jews and others is significant at the 0.001 per cent level. There are no differences, however, in the use of tobacco by religious preference among the controls (Table 10).

For the 134 pairs matched by age and use of tobacco, the proportion with clinically diagnosed liver cirrhosis is 22 per cent of the cases and only 12 per cent of the controls (Table 11). This difference is significant at the 5 per cent level. Alcohol consumption for these pairs is shown in Table 12. Among the cases, 44 per cent are heavy drinkers (1.6 ounces or more alcohol per day) as compared with only 24 per cent of the controls. This difference is significant at the 0.1 per cent level.

The use of tobacco among the 154 pairs matched by age and alcohol consumption is shown in Table 13. Among the cases, 23 per cent are heavy smokers (40 cigarette equivalents or more per day) as compared with 14 per cent of the controls. This difference is significant at the 5 per cent level.

No association of cancer of the mouth and pharynx is found with syphilis or with diabetes mellitus. There is no association with race. Among the total cases, 37 per cent are service workers and laborers as compared with 26 per cent of all controls. This difference is significant at the 0.01 per cent level.

Discussion

Both alcohol and tobacco consumption are associated with cancer of the mouth

Table 8—Religious Preference of Cases of Cancer of the Mouth and Pharynx and Age-Matched Controls, Veterans Administration Hospitals, New York City

	Cases		Controls	
	No.	%	No.	%
Protestants	196	32.8	182	30.4
Catholics	356	59.5[v]	301	50.3[v]
Jews	23	3.8[x]	96	16.1[x]
Others	4	.7	12	2.0
Not stated	19	3.2	7	1.2
Total	598	100.0	598	100.0

x—P <0.00001
v—P <0.001

Table 9—Alcohol Consumption Among Controls, by Religious Preference, Veterans Administration Hospitals, New York City

Alcohol per Day (oz)*	Protestants		Catholics		Jews	
	No.	%	No.	%	No.	%
None	34	18.7	46	15.3	35	36.4
<0.4	54	29.7	69	22.9	38	39.6
0.4-1.5	30	16.4	70	23.2	12	12.5
1.6+	40	22.0	74	24.6	2	2.1
Not stated	24	13.2	42	14.0	9	9.4
Total	182	100.0	301	100.0	96	100.0

* 0.4 oz=1 oz whiskey=4 oz wine=8 oz beer.

and pharynx. However, these habits are known to be related.[12-14] Of the 258 cases in this series who are heavy drinkers, 35 per cent are also heavy smokers; this is true for only 15 per cent of the 286 cases who are not heavy drinkers. A similar relationship is also demonstrated among the controls.

The manifest association of heavy drinking and heavy smoking made it necessary to test the independent roles of alcohol and tobacco. This was done by examining the data on alcohol consumption for pairs matched by tobacco use, and vice versa. The findings (Tables 12, 13) clearly indicate that both factors are independently associated with cancer of the mouth and pharynx.

The above conclusions are based on data obtained by the admitting physicians who, early in the admission procedure, elicited answers to routine questions on the use of tobacco and alcohol. Since past experience has indicated that interview data on the use of tobacco are relatively unbiased,[15,16] such data are presumed to be comparatively reliable. This presumption may not hold for the use of alcohol because social attitudes toward alcoholism plus the imminent reduction in veteran's benefits by the Veterans Administration to known or admitted alcoholics may induce respondents to report their drinking habits inaccurately. It is likely, therefore, that the data presented on alcohol consumption are underestimates.

The present study provides additional positive evidence on the relation of alcohol use and cancer of the mouth and

Table 10—Use of Tobacco Among Controls, by Religious Preference, Veterans Administration Hospitals, New York City

Cigarette Equivalents per Day*	Protestants		Catholics		Jews	
	No.	%	No.	%	No.	%
None	25	13.7	45	15.0	19	19.8
<20	37	20.3	45	15.0	15	15.6
20-39	68	37.4	105	34.8	32	33.3
40+	19	10.4	41	13.6	10	10.4
Not stated	33	18.1	65	21.6	20	20.9
Total	182	100.0	301	100.0	96	100.0

* 1 cigarette=½ pipeful=¼ cigar.

Table 11—Clinically Diagnosed Liver Cirrhosis Among Cases of Cancer of the Mouth and Pharynx and Controls Matched by Age and Use of Tobacco, Veterans Administration Hospitals, New York City

Liver Cirrhosis	Cases		Controls	
	No.	%	No.	%
Present	30	22.4[z]	16	11.9[z]
Absent	104	77.6	118	88.1
Total	134	100.0	134	100.0

z—P <0.05

Table 12—Alcohol Consumption Among Cases of Cancer of the Mouth and Pharynx and Controls Matched by Age and Use of Tobacco, Veterans Administration Hospitals, New York City

Alcohol per Day (oz)*	Cases		Controls	
	No.	%	No.	%
None	14	10.4	28	20.9
<0.4	28	20.9	41	30.6
0.4-1.5	25	18.7	24	17.9
1.6+	59	44.0[v]	32	23.9[v]
Not stated	8	6.0	9	6.7
Total	134	100.0	134	100.0

* 0.4 oz=1 oz whiskey=4 oz wine=8 oz beer.
v—P <0.001

Table 13—Use of Tobacco Among Cases of Cancer of the Mouth and Pharynx and Controls Matched by Age and Alcohol Consumption, Veterans Administration Hospitals, New York City

Cigarette Equivalents per Day*	Cases		Controls	
	No.	%	No.	%
None	13	8.4	22	14.3
<20	27	17.5	28	18.2
20-39	62	40.3	62	40.3
40+	35	22.7[z]	21	13.6[z]
Not stated	17	11.1	21	13.6
Total	154	100.0	154	100.0

* 1 cigarette=½ pipeful=¼ cigar.
z—P <0.05

pharynx. One type of evidence is the demonstrated association of these cancers with cirrhosis of the liver (Tables 1, 11). While it is true that not all cirrhosis of the liver is associated with chronic alcoholism,[17-24] most cases in a community like New York City are related to heavy drinking.[25,26] We consider it permissible, therefore, to use the presence of cirrhosis of the liver as a probable indicator of chronic alcoholism.

The other additional evidence relating cancer of the mouth and pharynx to alcohol use is the finding of a marked deficit of these cancers among Jews (Table 8). This deficit, which has also been reported by Wynder, Bross, and Feldman,[5] is difficult to explain on the basis of tobacco use, since in the population using these hospitals there is apparently little difference among religious groups in the use of tobacco (Table 10). Yet there is a marked difference in alcohol consumption in this population; heavy drinkers appear to be rare among Jews in the age groups covered by this study (Table 9). This finding is consistent with the known strong social disapproval of alcoholism among Jews.[27-31] The conclusion seems warranted that the deficit of cancer of the mouth and pharynx among Jews provides significant additional evidence of an association with heavy alcohol consumption.

Summary

A study of 598 cases of cancer of the mouth and pharynx, and an equal number of age-matched controls, admitted to the three Veterans Administration hospitals in New York City from 1953 to 1963, demonstrates that:

1. Cancer of the mouth and pharynx is associated with cirrhosis of the liver.
2. This cancer is associated independently with heavy alcohol consumption and heavy smoking.
3. A marked deficit in its occurrence is found among Jews.

These findings are consistent with the conclusion that both heavy alcohol consumption and heavy smoking are independently and significantly related to cancer of the mouth and pharynx.

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