

Tobacco, Alcohol, Diet, Occupation, and Carcinoma of the Esophagus¹

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ABSTRACT

Information on occupation, smoking, food and beverage consumption, and medical history were compared between 275 incident cases of carcinoma of the esophagus and 275 neighborhood controls who were matched to the cases on age (within 5 years), race, and sex. Tobacco use, mainly cigarette smoking, was a significant risk factor for carcinoma of the esophagus. Ex-smokers of cigarettes showed a reduced risk relative to those who continued to smoke, and current smokers of two or more packs per day displayed a higher risk than those who smoked less. Alcohol consumption was another significant risk factor for carcinoma of the esophagus; there was a highly significant trend with average daily dose of ethanol. Relative to controls, cases also consumed significantly more fried bacon or ham, less fresh fruits and raw vegetables, and were more likely to prefer white than whole grain bread. Finally, there was a significant association between carcinoma of the esophagus and long-term occupational exposure to metal dust; this association was largely confined to the lower one-third section of the esophagus.

INTRODUCTION

The incidence of esophageal carcinoma shows remarkable variation in its geographical distribution (1). In the high risk areas of Central Asia, dietary deficiencies are believed to play a major role in the pathogenesis of this disease (2). In the United States, carcinoma of the esophagus is relatively uncommon, although there is a severalfold difference in incidence between the black and the white population (3). In Los Angeles, the average annual age-adjusted incidence of esophageal cancer during 1972-1982 in black men, black women, white men, and white women was respectively 16.4, 4.9, 4.1 and 1.7 per 100,000 person-years. There is some evidence that the differential in risk of esophageal cancer between United States blacks and whites has continued to widen; in 1976-1980, the mortality rate in black males under age 55 was more than six times that in white males of similar ages (4). Consumption of tobacco and alcohol have been repeatedly shown to be major causes of carcinoma of the esophagus; it has been estimated that up to 80% of cases in industrialized countries could be attributed to exposure to these two environmental factors (1). However, it is not clear how much of the difference between United States blacks and whites can be explained by variations in exposure to tobacco and alcohol, and there is speculation that dietary deficiencies or occupational exposure might be responsible for some esophageal cancer. In this report, we describe a case-control study that was designed to study blacks and whites, to select representative cases and controls, and to search for previously unrecognized causes and the explanation for the observed racial difference.

MATERIALS AND METHODS

We studied histologically confirmed incident cases of carcinoma of the esophagus occurring among residents of Los Angeles County aged

20-64 years. Cases were identified through the Los Angeles County Cancer Surveillance Program (5), a population-based cancer registry which records all cases of cancer that are microscopically verified or mentioned on a death certificate. We attempted to recruit all cases diagnosed between January 1, 1975 and March 31, 1981. For all potential cases, we sought permission from the attending physician prior to contacting the patient or family for an interview. We began interviewing cases in April 1975 and terminated case recruitment in August 1981.

Controls were selected from the neighborhood of the cases' residence at the time of diagnosis. Using the house of each case as a reference point and proceeding in a systematic and invariable sequence, we canvassed up to 80 residential units to identify a control matched to the case on sex, year of birth (within 5 years), and race (non-Hispanic white, Hispanic white, black, Asian). We attempted to identify the sex, age, and race of the residents of each housing unit. A letter was left at each unattended unit to complete the census; two additional letters were sent at 3-week intervals if the previous one was unanswered. Our goal was to interview the first resident in each sequence who met the matching criteria. If the individual refused, the second eligible control in the sequence was asked to participate. If no potential control was identified within 80 housing units, then the race-matching criterion was relaxed. We excluded cases for whom no age- and sex-matched controls could be secured.

At the close of case recruitment, 488 eligible patients were identified by the cancer registry. We were unable to locate 77 cases, the physician refused to cooperate in 33 cases, the patient or family refused to cooperate in 87 cases, there was a language barrier in 8 cases, and we failed to secure a matched neighborhood control for 8 cases. Therefore, 275 (56% of eligible patients) pairs of cases and controls were included in the study. The matching criterion on race was not met for 25 controls. Most of the controls (239) were the first (161) or the second (78) eligible neighbors.

Almost all interviews were conducted in the homes of the respondents (98% of case interviews and 96% of control interviews). The remaining interviews were conducted by telephone at the request of the respondents. One hundred twenty-nine (47%) cases were interviewed directly; due to death of the patients, the remaining case interviews were conducted by proxy with close family members. Fifty-nine % of these proxy interviews were conducted with the spouse, and 37% were with a first degree relative. At the start of the study, we attempted to obtain a proxy interview from the analogous member of the control family if the index case was interviewed by proxy. This proved to be extremely difficult, so of the 146 controls matched to cases interviewed by proxy, only 55 could also be interviewed by proxy; the remainder were interviewed directly. The information from paired direct interviews was therefore analyzed separately in parallel to that from all pair interviews.

All interviews were administered by a single interviewer using a structured questionnaire. The interview took approximately 1 h and covered lifetime occupational history, vocational and avocational exposures to specific substances and industrial processes, smoking, alcohol and beverage history, usual frequency of consumption of a few broad food groups (beef, fried bacon or ham, deep fried foods, milk, eggs, barbecued or smoked meat, smoked fish, fresh fruits or raw vegetables, whole grain bread, and various ethnic categories of food), prior medical conditions, family history of certain diseases, and use of selected drugs. For cases, all events occurring after the diagnosis of cancer were eliminated. Similarly, events first occurring in the life of each control after the diagnosis of the index case were excluded.

Subjects were asked to recall specific workplace exposures, but such recollections are likely to be unreliable for those interviewed by proxy. Therefore, when we noted an association with reported metal dust exposure among directly interviewed pairs of cases and controls, we attempted to confirm the association in all cases and controls by using

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an exposure index which was derived from the titles of jobs previously held for a minimum period of 6 months. The assumption was that one is more likely to obtain accurate information regarding job titles than specific exposures from next of kin. Formulation of a matrix by which job titles are linked to categories of dust exposure has been described previously (6). Briefly, we reviewed occupational titles from the 1970 United States Bureau of Census Index and assigned each to 1 of 10 exposure categories: no exposure to particulates, exposed to metal dust only, mineral dust only, organic dust only, metal and mineral dusts, metal and organic dusts, mineral and organic dusts, smoke and exhaust, generally dusty jobs, and unknown exposure. Each subject was classified as exposed or unexposed according to whether the individual had ever held a job title assigned to that category. Duration of exposure was calculated by adding up the years worked in those jobs.

We used standard matched-pair methods (7) to analyze questionnaire data from the 275 pairs of cases and matched controls. Study variables were examined individually and then simultaneously for confounding and interaction effects. We used the exact binomial test on individual dichotomous variables. The multivariate conditional logistic regression method was used on single variables with more than two possible outcomes as well as for multivariate analysis. Pairs in which either the case or the control failed to answer the relevant question were eliminated from the analysis. All statistical significance levels (P values) quoted are two-sided. The method of Bruzzi *et al.* (8) was used to compute the population attributable risk. When we computed total ethanol intake from reported amounts of beer, sweet wine, table wine, and spirits, we used the following conversion factors: 1 can (12 fl oz) of beer contains 12.96 g; 1 glass (3.5 fl oz) of dinner wine contains 10.10 g; 1 glass (3.5 fl oz) of sweet wine contains 15.76 g; and 1 jigger (1.5 fl oz) of spirits contains 14.03 g of ethanol (9).

RESULTS

Sixty-eight % of the cases were men, 66% were non-Hispanic whites, and 88% were aged 50-64 years. Of the 87% cases with information on tumor location in the esophagus, the upper:middle:lower one-third ratio was 1:1.8:2.1. The predominant (88%) histological diagnosis was squamous cell carcinoma; the remaining cases were either adenocarcinomas (8%) or "carcinoma, unspecified" (4%). A comparison of the 275 cases studied with the 488 eligible cases showed the studied cases to be representative of all eligible patients with respect to sex, race, age, religion, place of birth, marital status, social class, subsite, and histology.

Cases and controls were similar in their age distribution. The mean age at diagnosis of the cases was 56.5 years, while that of the controls at date of diagnosis of the index case was 56.3 years. Cases and controls were comparable in their distributions by religion and by marital status. However, cases had significantly lower levels of education compared to controls (P for linear trend = 0.02). Whereas 17% of controls graduated from college, only 11% of cases did so.

Cigarette smoking was a strong predictor of risk for carcinoma of the esophagus (Table 1). Individuals who had ever smoked cigarettes regularly exhibited a significantly increased risk for carcinoma of the esophagus relative to those who had never used any tobacco products on a regular basis. Relative to those who continued to smoke, ex-smokers showed a reduced risk for carcinoma of the esophagus, and the magnitude of the reduction in risk increased with the length of time since cessation of smoking. Among current smokers, those smoking one pack or less per day had a lower risk for carcinoma of the esophagus relative to heavier smokers. There was no further increase in risk for esophageal carcinoma in current smokers smoking 3 or more packs per day relative to those smoking about 2 packs per day. Relative to nonusers of tobacco products, pipe and cigar smokers both had significantly elevated risks of

Table 1 Use of tobacco among cases and controls

	Directly interviewed pairs (N = 129)			All pairs (N = 275)		
	Ca/Co ^a	RR	95% CL	Ca/Co	RR	95% CL
Never used tobacco	11/31	1.0		18/73	1.0	
Cigarettes						
Ex-smoker						
Quit 20+ yr before	7/11	1.9	0.5, 6.6	11/22	1.9	0.7, 5.0
Quit 10-19 yr before	9/19	2.0	0.6, 7.2	21/31	3.8	1.5, 9.6
Quit 5-9 yr before	9/10	3.3	0.8, 12.8	11/18	3.9	1.3, 11.8
Quit 0-4 yr before	3/3	4.1	0.6, 28.6	10/7	6.5	1.7, 24.2
Current smoker						
1 pack/day or less	39/26	6.6	2.3, 19.3	64/56	7.2	3.1, 16.5
2 packs/day	32/14	9.1	2.9, 29.0	83/30	18.8	7.7, 46.1
3+ packs/day	14/8	5.1	1.5, 16.9	37/18	11.5	4.5, 29.8
Cigars						
1-4/day	10/8	4.9	1.4, 17.5	16/22	4.3	1.6, 11.7
5+/day	2/5	1.4	0.2, 8.9	6/7	5.5	1.5, 20.1
Pipe						
1-4/day	5/14	1.4	0.3, 5.8	12/25	3.0	1.1, 8.2
5+/day	6/5	4.9	1.1, 22.4	9/11	5.4	1.7, 17.1
Cigars and/or pipe only	4/6	2.2	0.4, 11.7	8/12	3.6	1.0, 12.3

^a Ca/Co, cases/controls; CL, confidence limits.

Table 2 Consumption of alcoholic beverages among cases and controls

	Directly interviewed pairs (N = 129)			All pairs (N = 275)		
	Ca/Co ^a	RR	95% CL	Ca/Co	RR	95% CL
Nondrinker	5/20	1.0		8/39	1.0	
Beer						
Weekly	32/19	8.7	2.5, 30.4	60/46	6.8	2.8, 16.6
1-6 cans/day	49/39	6.7	2.1, 21.7	106/72	8.4	3.5, 20.0
7+ cans/day	13/9	7.7	1.8, 32.9	28/14	12.1	4.1, 35.4
Sweet wine						
Weekly	29/37	2.8	0.9, 9.1	45/71	2.7	1.1, 6.5
1-3 glasses/day	9/3	11.0	2.0, 60.8	20/10	13.7	4.1, 45.9
4+ glasses/day	9/2	30.6	2.9, 326.3	31/6	67.5	12.5, 363.2
Dinner wine						
Weekly	45/46	4.0	1.3, 12.5	82/97	3.8	1.6, 9.0
1-3 glasses/day	12/13	3.5	0.9, 12.9	23/20	5.2	1.9, 14.2
4+ glasses/day	2/1	11.9	0.8, 168.9	9/1	47.5	5.1, 440.8
Spirits						
Weekly	46/64	3.2	1.0, 9.7	91/136	3.4	1.5, 7.8
1-3 shots/day	36/25	7.2	2.1, 24.7	62/44	7.3	2.9, 18.6
4+ shots/day	38/16	13.7	3.7, 51.3	98/35	16.3	6.3, 42.1
Average daily intake of ethanol (g)						
less than 40	41/55	2.9	0.9, 9.5	69/122	2.6	1.1, 6.2
40-79	34/28	4.8	1.5, 14.9	67/56	5.6	2.3, 13.4
80-119	19/12	7.4	2.0, 27.9	42/19	12.4	4.4, 34.9
120+	30/14	10.3	2.8, 38.0	76/27	15.5	5.9, 41.1

^a Ca/Co, cases/controls; CL, confidence limits.

esophageal carcinoma. This elevation in risk remained when we restricted exposure to cigars and/or pipe in the absence of cigarettes (Table 1).

Consumption of alcoholic beverages was another strong predictor of risk for carcinoma of the esophagus (Table 2). Relative to individuals who did not drink regularly, regular drinkers (those who drank at least once a week) of beer, sweet wine, dinner wine, and spirits all showed a highly significant dose-response relationship with usual quantities of consumption. Increased risks were observed when exposures were limited to beer only, sweet wine only, and spirits only (there were no cases who drank dinner wine only). The multivariate conditional logistic regression method was used to examine the effect of individual beverages (each converted to g of ethanol) in the presence of all other alcoholic beverages. Consumption of beer, sweet wine, and spirits was found to exert significant independent effects on risk for carcinoma of the esophagus. Of those three types of alcoholic beverages, spirits showed the strongest and beer the weakest association with carcinoma of the esophagus when the amount of ethanol was held constant. For all pairs, the regression coefficients for spirits, sweet wine, and beer per 10 g increase in ethanol content were 0.173, 0.147,

Table 3 Selected food consumption among cases and controls

	Directly interviewed pairs (N = 129)			All pairs (N = 275)		
	Ca/Co ^a	RR	95% CL	Ca/Co	RR	95% CL
Beef						
1/wk or less	8/11	1.0	0.3, 2.9	20/21	1.3	0.6, 2.7
2-4/wk	79/67	1.5	0.8, 2.6	169/150	1.5	1.0, 2.3
5+/wk	42/51	1.0		78/96	1.0	
Fried bacon or ham						
1/wk or less	67/79	1.0		133/159	1.0	
2-4/wk	37/41	1.1	0.6, 2.0	91/81	1.4	0.9, 2.1
5+/wk	24/8	3.4 ^b	1.4, 8.2	41/25	2.0 ^c	1.1, 3.5
Milk						
1/wk or less	39/50	1.0		93/97	1.0	
2-4/wk	19/17	1.4	0.7, 3.0	38/37	1.1	0.6, 1.8
5+/wk	71/62	1.4	0.8, 2.4	138/135	1.1	0.7, 1.6
Eggs						
1/wk or less	26/28	1.0		58/54	1.0	
2-4/wk	58/61	1.0	0.5, 2.0	139/132	1.0	0.6, 1.5
5+/wk	44/39	1.2	0.6, 2.3	71/82	0.8	0.5, 1.3
Barbecued or smoked meat						
1/wk or less	120/120	1.0		237/249	1.0	
2+/wk	9/9	1.0	0.4, 2.7	31/19	1.7	0.9, 3.0
Fresh fruits or raw vegetables						
1/wk or less	13/8	2.5 ^c	0.9, 6.6	33/20	2.3 ^d	1.2, 4.4
2-4/wk	51/27	2.5	1.4, 4.5	101/63	2.2	1.5, 3.2
5+/wk	62/91	1.0		133/184	1.0	
Bread preference						
Whole grain	35/60	1.0		67/113	1.0	
No preference	38/29	2.0	1.1, 3.7	82/67	2.1	1.3, 3.4
White	56/40	2.4 ^c	1.3, 4.3	121/90	2.4 ^d	1.6, 3.7

^a Ca/Co, cases/controls; CL, confidence limits.^b Linear trend $P < 0.05$, but > 0.01 .^c Linear trend $P < 0.01$, but > 0.001 .^d Linear trend $P < 0.001$.

and 0.079, respectively. For directly interviewed pairs, the corresponding regression coefficients were 0.183, 0.124, and 0.025, respectively. When all sources of exposure to alcohol were summed to form a single index (average daily intake of ethanol), a highly significant trend was observed between the alcohol index and carcinoma of the esophagus (all pairs and directly interviewed pairs, $P < 0.0001$).

Table 3 presents the distribution of consumption frequency of various food groups in cases and controls. Subjects were asked to choose between three specified categories of frequency: once a week or less, two to four times a week, and five or more times a week. Cases and controls were similar in their frequency of consumption of beef, milk, and eggs. However, cases had significantly higher frequency of consumption of fried bacon or ham, and significantly lower frequency of consumption of fresh fruits or raw vegetables relative to controls. Also, significantly more cases than controls preferred white over whole grain bread. A multivariate analysis of these three dietary factors showed a significant association between each factor and risk for carcinoma of the esophagus after adjusting for the other two. We also examined the effects of smoking, drinking, and diet by tumor location (upper, middle, and lower third of the esophagus). No appreciable differences were observed.

When we compared the prevalence of reported exposure to metal dust on the job between directly interviewed cases and controls, we observed a significant excess among cases (42 cases and 29 controls, $RR^3 = 2.2$, 95% confidence limits = 1.1, 4.5). Exposure to every kind of dust (beryllium, chromium and chromates, nickel, other metal dusts) was more prevalent among cases than controls. The association was particularly strong for exposure to beryllium. Twelve cases and only two controls claimed a history of beryllium exposure on the job ($RR = 6.0$, 95% confidence limits = 1.4, 37.5). Initial exposures of these 12 cases all occurred at least 19 years before the diagnosis

of cancer; the mean interval was 30.8 years before diagnosis. Nine cases had been exposed for 15 or more years; the mean duration for all 12 cases was 19.8 years. Ten cases (and both controls) also reported exposure to other kinds of metal dust on those same jobs which exposed them to beryllium. There was no association between reported occupational exposure to asbestos and esophageal carcinoma risk (18 cases and 25 controls, $RR = 0.6$, $P = 0.28$).

Table 4 shows the difference between cases and controls in their prevalence of exposure to various kinds of dust. Exposure information was derived from job titles ever held by the case or the control for 6 months or longer before diagnosis of the case (see "Materials and Methods" for a more detailed description). Occupational exposure to metal dust was a significant risk factor for carcinoma of the esophagus. There was no association with other kinds of dusts. Similar results were obtained when jobs that started within 10 years of diagnosis of the case were excluded.

There was a duration-response relationship between exposure to metal dust and risk for carcinoma of the esophagus. The results were similar whether or not we excluded jobs that were started shortly prior to diagnosis of the case. Table 5 presents the results based on exclusion of jobs started within the prior 10 years. In all instances, higher risk was associated with longer duration of exposure. The association was also subsite specific, the increased risk was largely confined to the lower one-third section of the esophagus (Table 5).

The above risk factors were further examined within specific sex and race groups (white males, white females, black males, black females). Albeit the small numbers in the subgroups, there was remarkable consistency in the strength of the associations among the four groups. We also examined the risk factors within the 161 case-control pairs in which the first eligible control participated; similar results were obtained. We used the multivariate conditional logistic regression method to examine the joint effect of the various risk factors (Table 6). Each factor remained significant after simultaneous adjustment for the other factors and the highest level of education.

Aside from the risk factors reported above, cases were signif-

Table 4 Occupational exposure to dust among cases and controls (exposure information derived from job titles)

	Directly interviewed pairs (N = 129)			All pairs (N = 275)		
	Ca/Co ^a	RR	95% CL	Ca/Co	RR	95% CL
Any dust	93/88	1.3	0.7, 2.5	189/184	1.1	0.7, 1.7
Metal	47/27	2.7	1.4, 5.4	84/63	1.6	1.0, 2.5
Mineral	26/24	1.1	0.6, 2.3	51/50	1.0	0.6, 1.7
Organic	35/42	0.8	0.5, 1.3	63/82	0.7	0.4, 1.0
Smoke and exhaust	15/24	0.6	0.3, 1.2	39/43	0.9	0.5, 1.4
Exposed, generally dusty jobs	61/52	1.4	0.8, 2.3	125/116	1.2	0.8, 1.7

^a Ca/Co, cases/controls; CL, confidence limits.

Table 5 Duration of metal dust exposure started 10+ years before diagnosis of the case (exposure information derived from job titles)

	Directly interviewed pairs (N = 129)			All pairs (N = 275)		
	Ca/Co ^a	RR	95% CL	Ca/Co	RR	95% CL
No exposure	83/103	1.0		198/215	1.0	
1-19 yr	27/20	2.0	1.0, 4.0	46/50	1.1	0.7, 1.7
20+ yr	19/6	4.5	1.6, 12.8	28/7	4.6	1.9, 11.3
Subsite: lower one-third						
No exposure	31/40	1.0		77/87	1.0	
1-19 yr	6/6	1.6	0.5, 5.8	11/16	0.9	0.4, 2.0
20+ yr	13/4	4.6	1.2, 17.6	19/4	5.8	1.7, 20.1

^a Ca/Co, cases/controls; CL, confidence limits.³ The abbreviation used is: RR, relative risk.

Table 6 Adjusted regression coefficients for various risk factors of carcinoma of the esophagus

	Directly interviewed pairs (N = 129)		All pairs (N = 275)	
	Adjusted B ^a	Two-sided P	Adjusted B ^a	Two-sided P
Average daily use of tobacco (g)	0.018	0.032	0.025	0.000
Average daily intake of ethanol (g)	0.008	0.005	0.012	0.000
Fried bacon or ham ^b	0.562	0.017	0.489	0.008
Fresh fruits or raw vegetables ^b	0.582	0.033	0.419	0.024
Bread preference ^c	0.215	0.240	0.339	0.024
Duration of metal dust exposure started 10+ yr before diagnosis of case (yr)	0.033	0.096	0.043	0.017

^a Parameters estimated from logistic regression model which included highest level of education and all factors in the table.

^b Coded levels are: 1/wk or less = 1; 2-4/wk = 2; 5+/wk = 3.

^c Coded levels are: whole grain = 1; no preference = 2; white = 3.

icantly more likely than controls to report a history of stomach ulcer, frequent sore throat (more than 2 times per year), chronic cough, and regular use of antibiotics. Frequency of use of table salt and condiment was significantly higher in cases than in controls. The relative weights (10 years before) of cases were significantly lower than those of controls. Among females, cases achieved menopause significantly earlier and were significantly less likely to have hormone replacement therapy than controls. None of these associations remained significant after adjustment for highest level of education, tobacco use, consumption of alcohol, bacon or ham, and fresh fruits or raw vegetables; preference for white *versus* whole grain bread, and occupational exposure to metal dust.

There was no association between carcinoma of the esophagus and frequency of tea consumption. The reported temperature of the tea and the manner it was drunk (sipped slowly, gulped quickly, neither) were not different between cases and controls. Similarly, the frequency, temperature, type (caffeinated, decaffeinated, both) and manner of consumption of coffee was not related to carcinoma of the esophagus.

DISCUSSION

The role of tobacco and alcohol use in the etiology of carcinoma of the esophagus is well established. Elevated risk in smokers relative to nonsmokers has been consistently demonstrated in cohorts of United States Veterans (10, 11), American Cancer Society volunteers (12), British physicians (13), members of labor unions (14), and representative residents of Japan (15). As a group, alcoholics suffer a high risk (16-18), just as religious nondrinkers enjoy a low risk (19, 20); moreover, a significant independent effect of alcohol consumption was observed in the Japanese prospective cohort (21). Case-control studies conducted in New York (22), Washington, DC (23), Puerto Rico (24), Uruguay (25), Brazil (26), France (7, 27), and Singapore (28) have provided further evidence of the close and independent roles of tobacco and alcohol in the etiology of carcinoma of the esophagus.

In contrast to most earlier case-control studies which are either hospital based or have relied exclusively on surrogate interviews, the present study compares representative cases with general population controls and about one-half of the cases studied were interviewed directly. The magnitude of risk estimates from use of tobacco and alcohol in this study are in general agreement with those of earlier studies. We found ex-smokers to have a reduced risk for carcinoma of the esophagus

relative to current smokers, and current heavy smokers displayed a higher risk than current light smokers. There was no further increase in risk with daily dose of cigarettes beyond two packs. Alcohol consumption, on the other hand, exhibited a monotonic increase in risk within the reported range of daily consumption. We estimate that 93% of our cases were associated with exposure to tobacco and alcohol either singly or jointly.

We observed differential risks for carcinoma of the esophagus by different types of alcoholic drinks. For any given level of ethanol intake, the risk from spirits was more than two times that from beer, with risk from wine intermediate between those from spirits and beer. Our findings support those of other studies. In Japan (21), the excess risk associated with alcohol was highest for whiskey and shochu (a local liqueur) and lowest for beer. In Washington, DC (23), the excess risk was greatest for hard liquor, particularly whiskey or bourbon, and lowest for beer. In New York, Wynder and Bross (22) reported a higher risk for heavy whiskey drinkers than for heavy beer drinkers among those smoking between 16 and 34 cigarettes per day. In Puerto Rico (24), there was little excess risk among those drinking solely beer; among drinkers of spirits, the greatest risk was in those who took drinks straight.

Both descriptive and analytical studies have implicated dietary deficiencies as a risk factor for carcinoma of the esophagus. High-risk populations have been noted to be deficient in vitamins, trace metals, and essential amino acids. Case-control studies in diverse populations have reported significantly lower intake of food groups high in micronutrients among cases relative to controls (1). In the United States, Wynder and Bross (22) reported that mostly white cases in New York consumed significantly less milk, and fewer green and yellow vegetables than controls. In a study of black men in the Washington, DC area, Pottern *et al.* (23) observed 2-fold increased risks among individuals in the lowest, compared to the highest, tertile of consumption of each of three food groups; fresh or frozen meat and fish, dairy products and eggs, and fruits and vegetables. Recently, two studies in Europe (29, 30) showed significant negative associations between consumption of fresh meats, vegetables, and fruits and esophageal cancer risk.

Our cases consumed significantly fewer fresh fruits and raw vegetables relative to controls, in agreement with the results of previous studies. On the other hand, we did not find any difference in consumption of beef, milk, or eggs between cases and controls. We observed a decreased risk of esophageal carcinoma among individuals who preferred whole grain bread, but this is likely to be a surrogate measure of better nutritional status rather than a direct measure of a specific nutrient deficiency. The crudeness of our dietary questions preclude any examination of risk of esophageal carcinoma by level of dietary micronutrients.

We demonstrated a significant dose-response relationship between intake frequency of fried bacon or ham and risk of esophageal carcinoma. These cured meat products contain nitrosamines (31), many of which are potent inducers of malignant tumors, including esophageal carcinomas, in animals (32, 33). There is suggestive epidemiological evidence that nitrosamines are involved in the etiology of esophageal carcinoma. Preformed nitrosamines and their precursors (nitrite, nitrate, and secondary amines) were detected in various common foods and drinking water consumed in Linxian County, China, an extremely high-risk area for esophageal cancer (34-39), and residents of Linxian were found to have significantly higher urinary levels of nitrate and several *N*-nitrosamino acids than

residents of Fanxian, a nearby county with relatively low rates of esophageal cancer (40).

Occupational exposure to metal dust, especially beryllium, was found to be a risk factor for carcinoma of the lower one-third of the esophagus. The esophagus is potentially exposed to inhaled dust particles since dust deposited in the respiratory tract is ultimately cleared by the mucociliary apparatus and is swallowed. A number of metals, including inorganic arsenic, chromium, and nickel, have been shown to be risk factors for respiratory cancers in humans (41, 42), lending some credibility to the hypothesis that the observed association between esophageal cancer and exposure to metal dusts is a causal one.

Two studies have suggested that plumbers and pipefitters are at an increased risk of esophageal cancer (43, 44). We found a nonsignificant excess of plumbers and pipefitters among the cases. Six cases relative to one control were previously employed as plumbers or pipefitters ($P = 0.13$). All six cases were first employed as plumbers or pipefitters at least 25 years prior to the diagnosis of cancer. The duration of employment of these cases was 3 (2 cases), 5, 9, 22, and 35 years, respectively. In addition to metal dusts and fumes, plumbers and pipefitters are potentially exposed to known or suspected carcinogenic substances such as asbestos, tar, benzene, and chlorinated aliphatic solvents.

There have been reports that populations heavily exposed to asbestos have experienced an increased risk of esophageal cancer (45, 46). We did not find an association between asbestos exposure and esophageal carcinoma risk.

Although this study was population based, the participation rate was relatively low (56% of eligible patients). In addition, due to the rapidly fatal nature of the disease, only 47% of cases who participated in the study were interviewed directly. The generality and validity of our findings, therefore, needs to be critically evaluated. A comparison of the 275 cases studied with the 488 eligible cases showed the two groups to be comparable with respect to all items routinely collected by the Cancer Surveillance Program (sex, race, age, religion, place of birth, marital status, social class, subsite, and histology), and it seems reasonable to assume that the study cases are representative of eligible patients. A comparison of results based on all pairs with those based on only directly interviewed pairs found them to be consistent; the 95% confidence intervals associated with RRs from the two sets are largely overlapping. Interview status (direct *versus* proxy) does not appear to have affected the quality of the information collected. This is not entirely surprising since the information sought relates to past events and life-style factors familiar to spouses and first degree relatives. We also noted a high degree of consistency in the strength of the observed associations across sex-race strata, and this internal consistency of our data provides some assurance that these findings reflect real differences.

Among black male controls, 53% were current smokers, 33% consumed more than 80 g of ethanol per day, 20% ate fried bacon or ham at least 5 times per week, 50% had fresh fruits and raw vegetables less frequently than 5 times a week, and 33% preferred whole grain bread. In contrast, the corresponding percentages among the white male controls were 37, 19, 8, 25, and 44%. Our study, therefore, suggests that differences in smoking, drinking, and dietary habits all contribute to the differential risk of esophageal carcinoma between United States blacks and whites. There is no evidence that occupational exposure to metal dust plays a role in this black-white risk difference.

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