



Original article

Scand J Work Environ Health [2001;27\(4\):233-239](#)

doi:10.5271/sjweh.610

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by [Elci OC](#), [Dosemeci M](#), [Blair A](#)

Affiliation: Occupational Epidemiology Branch, National Cancer Institute, 6120 Executive Boulevard, EPS 8111, MSC 7240, Rockville, MD 20852–7240, USA. elcio@mail.nih.gov

The following articles refer to this text: [2002;28\(4\):278-284](#);
[2006;32\(4\):270-275](#)

Key terms: [cancer](#); [case-control study](#); [case-referent study](#); [laryngeal cancer](#); [larynx](#); [occupation](#); [occupational epidemiology](#); [risk](#); [Turkey](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/11560337



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Occupation and the risk of laryngeal cancer in Turkey

by Omur Cinar Elci, MD,¹ Mustafa Dosemeci, PhD,¹ Aaron Blair, PhD¹

Elci OC, Dosemeci M, Blair A. Occupation and the risk of laryngeal cancer in Turkey. *Scand J Work Environ Health* 2001;27(4):233—239.

Objectives A hospital-based case-referent study was conducted in Turkey to provide further information on occupational risk factors and laryngeal cancer.

Methods Among 7631 cancer cases seen at an oncology treatment center between 1979 and 1984, 958 laryngeal cancer cases were identified among men. Occupational history, tobacco and alcohol use, and demographic data were obtained from patients with a standardized questionnaire. Special 7-digit standard occupational and industrial codes were created to classify the job and industrial titles of the subjects. After exclusions, 940 laryngeal cancer cases and 1519 referents were available for study. Age-, smoking- and alcohol-adjusted odds ratios (OR) and 95% confidence intervals (95% CI) were calculated.

Results Excess laryngeal cancer occurred among guards (OR 1.5, 95% CI 1.1—2.1), production supervisors (OR 1.8, 95% CI 1.1—3.1), textile workers (OR 1.9, 95% CI 1.2—3.3), drivers (OR 1.7, 95% CI 1.1—2.4), construction workers (OR 1.7, 95% CI 1.2—2.6), and workers in grain mills (OR 3.1, 95% CI: 1.3—7.6), trade unions (OR 3.6, 95% CI: 1.1—11.7) and local government services (OR 4.7, 95% CI 1.7—12.5). Supraglottic cancer was excessive among the textile workers, construction workers, and local government laborers, all with potential dust exposure. The risks of the general managers, electricians, and workers from industries such as pharmaceutical production, industrial machinery production, electric utilities, and retail services were lower than expected.

Conclusions The risk of laryngeal cancer was associated with several occupations, and supraglottic larynx cancer appears to be more common among workers in dusty occupations and industries.

Key terms cancer, case-control study, case-referent study, larynx, occupational epidemiology.

Laryngeal cancer is the second most common respiratory cancer after lung cancer worldwide (1). It is relatively uncommon in most countries but is the second leading cancer among men in Turkey (2). Larynx cancer was responsible for about 7.0% of the deaths among men in Turkey in the 1970s (3). Recent statistics of the International Agency for Research on Cancer (IARC) showed that the larynx remains an important cancer site in Turkey, with an age-standardized incidence rate of 11.52 per 100 000 among men. This incidence rate is almost two times higher than the world rate (5.69) and nearly 1.5 times higher than that of North America (6.80) and western Europe (8.87) (figure 1) (4). It is

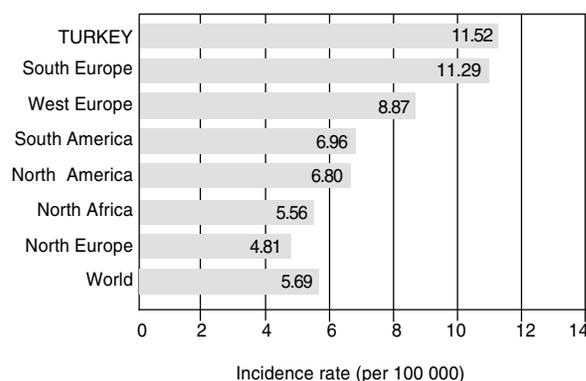


Figure 1. Age-adjusted incidence rate of laryngeal cancer in 1990 (4).

¹ Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville Maryland, United States.

Reprint requests to: Dr Omur Cinar Elci, Occupational Epidemiology Branch, National Cancer Institute, 6120 Executive Boulevard, EPS 8111, MSC 7240, Rockville, MD 20852—7240, USA. [E-mail: elcio@mail.nih.gov]

generally accepted that laryngeal cancer is highly related to alcohol and tobacco consumption (1, 5), but occupational and environmental factors also play a role (1, 5, 6). Inorganic acids (7–11), polycyclic aromatic hydrocarbons (PAH) (12), nickel (13, 14), solvents (15), paints, grease, metalworking fluids (16, 17), gasoline, diesel oil and mineral oil (18), and pesticides (11,13) have been linked with laryngeal cancer. Exposure to various dusts (19), including cement and metal (14), silica (20), and welding fumes (21), has been associated with an increased risk of cancer of the larynx.

Few studies investigating laryngeal cancer and occupational risk factors have taken place in developing countries (10, 22). Differences in life-style factors, work conditions, and occupational exposures could affect occupational relationships. A hospital-based case-referent study was conducted in Turkey to provide additional information on occupational risk factors and laryngeal cancer in a developing country.

Subjects and methods

The study population comprised patients of the oncology treatment center of the Social Security Agency Okmeydani Hospital between 1979 and 1984. This is one of the largest cancer therapy centers in Istanbul, Turkey. It provides treatment to most workers in the Marmara region, which is the northwest part of Turkey, and also to some workers in other regions. Upon admission to the hospital, all the patients responded to a standardized questionnaire administered by trained interviewers seeking information on occupational history and tobacco and alcohol use. Details of the data collection method have been explained elsewhere (22, 23). Among the 7631 cancer cases admitted to this hospital between 1979 and 1984, there were 958 diagnosed laryngeal cancer cases.

The diagnostic records of the patients were reviewed by an oncologist from the hospital for diagnostic veri-

fication and then coded according to the International Classification of Diseases for Oncology (ICD-O) classification system (24). Four-digit ICD-O codes of 161.0, 161.1, 161.2, and 161.9 were selected for the classification of tumor location. Because of the limited numbers, cases with subglottic (code 161.2) and nonclassified (code 161.9) cancers were combined for this analysis (N=275, 29.3%), while glottic (code 161.0, N=227, 24.1%) and supraglottic tumors (code 161.1, N=438, 46.6%) were considered separately.

Due to the limited number of cases (N=7), women were excluded from the analysis. The subjects with incomplete information on age, smoking, alcohol consumption, job titles, industry titles, and tumor site were also excluded, leaving 940 laryngeal cancer cases and 1519 other cancer referents. All patients with Hodgkin's disease (N=202), soft-tissue sarcoma (N=130), and cancers of nonmelanoma skin (N=657), testis (N=219), bone (N=66), male breast (N=34), and a small series of noncancer subjects (N=211) admitted to the hospital during the period 1979–1984 were included in the reference series. These cancers were selected for this analysis because they are thought not to share similar etiologic factors with laryngeal cancer. Two hundred and eleven noncancer patients initially misdiagnosed as cancer and admitted to the Okmeydani Hospital for treatment, where they were re-evaluated and diagnosed as other benign pathologies, were also used as referents.

Occupations and industries were coded using a modification of the 4-digit Standard Occupational Classification (SOC) and Standard Industrial Classification (SIC) coding system used in the United States (25). Special 7-digit SOC and SIC codes were created to provide more detailed information on jobs and industries. For example, "assemblers" (SOC code 7720) is one of the largest occupational groups that include automobile assemblers (modified SOC code 7720–018), box makers (modified SOC code 7720–118), electronic assemblers (modified SOC code 7720–207), mechanical assemblers (modified SOC code 7720–327), as well as others. The 7-digit modified coding system gave us a chance to evaluate our subjects in more-detailed specific groups. Among all the laryngeal cancers, 880 (93.6%) occurred in blue-collar workers [odds ratio (OR) 2.4, 95% confidence interval (95% CI) 1.7–3.3].

All the occupational and industrial groups with five or more cases of laryngeal cancer were selected for analysis. The Mantel-Haenszel analysis was used to determine the odds ratios and 95% confidence intervals, as adjusted for age (<45, 45–54, 55–64, and ≥65 years), smoking (ever-never), and alcohol consumption (ever-never) using SPSS (Statistical Package for the Social Sciences) version 9.0. The distribution of the cases and referents by confounding factors (age, tobacco use and alcohol consumption) is shown in table 1. The mean age

Table 1. Distribution of the cases and referents by age groups, smoking, and alcohol consumption.

	Cases		Referents	
	N	%	N	%
Age groups				
< 45 years	194	20.6	663	43.7
45–54 years	363	38.6	374	24.6
55–64 years	246	26.2	262	17.2
≥ 65 years	137	14.6	220	14.5
Smokers	611	65.0	890	58.6
Alcohol users	202	21.5	185	13.4
Total	940	100.0	1519	100.0

was 52.9 (SD 10.3) years for the cases and 47.1 (SD) 15.4) years for the referents. While 73.9% of the cases were smokers and 24.5% regularly consumed alcohol, smoking and alcohol consumption were less common among the referents, 58.6% and 13.4%, respectively. The age-adjusted odds ratio for laryngeal cancer among the smokers and alcohol consumers was 1.7 (95% CI 1.4–2.1) and 2.0 (95% CI 1.6–2.6), respectively. Given that we did not have pack·year and bottle·year information for up to 50% of the subjects who reported smoking or drinking alcohol, we used ever-never data in our analyses. For those with pack-year or bottle-year information, the odds ratios for laryngeal cancer did not differ from the odds ratios for the ever-never data.

Results

We calculated the odds ratios for all occupations and industries with at least five laryngeal cancers (ie, 31

Table 2. Risk of laryngeal cancer by occupation. (OR = odds ratio, 95% CI = 95% confidence interval)

Occupation	Cases (N)	OR ^a	95% CI
Fire fighters	7	3.9	0.7–21.5
Street cleaners	5	2.8	0.5–14.3
Ticket sellers	7	2.1	0.6–7.8
Food production workers	8	2.0	0.6–7.1
Textile workers	37	1.9	1.2–3.3
Production supervisors	38	1.8	1.1–3.1
Construction workers	66	1.7	1.2–2.6
Drivers	75	1.7	1.1–2.4
Excavators	6	1.7	0.6–5.2
Pressers	6	1.7	0.5–5.4
Extractive workers	31	1.6	0.9–2.8
Guards	71	1.5	1.1–2.1
Bakers	33	1.4	0.8–2.4
Painters	11	1.4	0.6–3.6
Laborers	25	1.1	0.6–2.1
Movers and handlers	22	1.0	0.6–1.8
Boilers	18	1.0	0.6–1.9
Farmers	12	1.0	0.5–2.3
Machine operators	8	1.0	0.4–2.5
Cleaners	33	0.9	0.6–1.5
Foundry workers	7	0.9	0.3–2.2
Mechanics	28	0.8	0.5–1.3
Office clerks	20	0.8	0.4–1.5
Furnace, oven operators	8	0.8	0.3–2.1
Lathe operators	9	0.8	0.3–1.9
Waiters	6	0.7	0.3–2.1
Sailors	11	0.6	0.3–1.3
Accountants	11	0.5	0.3–1.1
Welder	7	0.5	0.2–1.3
General managers	14	0.4	0.2–0.9
Electricians	5	0.3	0.1–0.8

^a Adjusted for age, smoking, and alcohol consumption.

occupations and 54 industries). Five occupations had an excess risk of laryngeal cancer [textile workers (OR 1.9, 95% CI 1.2–3.3), production supervisors (OR 1.8, 95% CI 1.1–3.1), construction workers (OR 1.7, 95% CI 1.2–2.6), drivers (OR 1.7, 95% CI 1.1–2.4), and guards (OR 1.5, 95% CI 1.1–2.1)] (table 2). The relative risks for the general managers (OR 0.4, 95% CI 0.2–0.9) and electricians (OR 0.3, 95% CI 0.1–0.8) were less than 1.0. We further analyzed production supervisors and guards by industry because occupational risk factors among these groups are mostly industry-based. The excess risk that occurred among production supervisors was primarily restricted to a few industries, including textile (OR 5.8, 95% CI 0.6–53.5), paper (OR 2.0, 95% CI 0.3–12.9), and oil production (OR 1.5, 95% CI 0.1–33.7). The same approach to guards showed slightly increased risks for guards working in highway construction (OR 1.3, 95% CI 0.8–1.9) and the textile industry (OR 1.2, 95% CI 0.7–1.8).

The odds ratios are shown in table 3 by tumor site and occupation. There were elevated risks of glottic cancer for drivers (OR 2.2, 95% CI 1.3–3.8) and guards (OR 1.9, 95% CI 1.2–3.2). Supraglottic cancer was excessive among the textile workers (OR 2.6, 95% CI 1.4–4.8) and construction workers (OR 1.9, 95% CI 1.2–3.1).

Table 3. Risk of laryngeal cancer by cancer site for selected occupations. (OR = odds ratio, 95% CI = 95% confidence interval)

Occupation	Cases (N)	OR ^a	95% CI
Textile workers			
Glottis	4	0.9	0.3–2.6
Supraglottis	22	2.6	1.4–4.8
Other	11	2.0	0.9–4.2
Production supervisors			
Glottis	9	1.7	0.7–4.0
Supraglottis	15	1.7	0.8–3.3
Other	14	2.6	1.2–5.3
Construction workers			
Glottis	10	1.2	0.6–2.5
Supraglottis	34	1.9	1.2–3.1
Other	22	2.0	1.1–3.5
Drivers			
Glottis	22	2.2	1.3–3.8
Supraglottis	27	1.2	0.7–1.9
Other	26	1.8	1.1–3.1
Guards			
Glottis	24	1.9	1.2–3.2
Supraglottis	28	1.2	0.8–2.0
Other	19	1.3	0.8–2.3
General managers			
Glottis	4	0.5	0.2–1.6
Supraglottis	5	0.4	0.2–1.2
Other	5	0.3	0.1–1.3
Electricians			
Glottis	–	–	–
Supraglottis	4	0.5	0.1–1.6
Other	1	0.2	0.0–1.8

^a Adjusted for age, smoking, and alcohol consumption.

Table 4. Risk of laryngeal cancer by industry. (OR = odds ratio, 95%CI = 95% confidence interval)

Industry	Cases (N)	OR ^a	95% CI
Local government services	15	4.7	1.7—12.5
Trade Unions	15	3.6	1.1—11.7
Grain mill	14	3.1	1.3—7.6
Educational services	8	2.7	0.8—8.7
Knitting mill	9	2.1	0.7—6.1
Cement production	6	1.8	0.5—6.7
Repair services	8	1.7	0.6—4.8
Warehousing	8	1.7	0.5—5.8
Highway construction	38	1.6	0.9—2.6
Tea production	18	1.6	0.8—3.2
Water supply	20	1.5	0.7—3.2
Gasoline	15	1.5	0.6—3.5
Grocery	13	1.5	0.5—3.9
Nonferrous metal industry	10	1.4	0.6—3.3
Paint production	6	1.4	0.4—5.3
Hotels	5	1.4	0.3—5.8
Building construction	56	1.3	0.9—2.0
Clay production	13	1.3	0.6—3.2
Oil production	10	1.3	0.5—3.2
Textile mill	61	1.2	0.9—1.7
Bakery production	20	1.2	0.6—2.4
Eating places	17	1.2	0.6—2.4
Government	46	1.1	0.7—1.7
Tobacco production	16	1.1	0.6—2.4
Fabricated metal industry	15	1.1	0.5—2.5
Highway transport	18	1.1	0.5—2.3
Sugar production	15	1.1	0.5—2.6
Liquor production	12	1.1	0.5—2.6
Motor vehicles	9	1.1	0.4—2.6
Chemical production	11	1.1	0.4—2.8
Forestry	8	1.1	0.4—2.9
Yarn mill	27	1.0	0.5—1.7
Railroad construction	16	1.0	0.5—2.1
Nonmetal mining	7	1.0	0.4—2.6
Metal mining	7	1.0	0.3—3.0
Glass production	7	1.0	0.3—3.1
Paper production	17	0.9	0.5—1.9
Rubber production	12	0.9	0.4—1.8
Leather production	7	0.9	0.3—2.2
Passenger transport, travel	9	0.9	0.3—2.6
Motion pictures	7	0.9	0.3—3.0
Coal mining	42	0.8	0.5—1.3
Agriculture	7	0.8	0.3—2.4
Metal industry	21	0.7	0.4—1.3
Hospitals	12	0.7	0.3—1.5
Furniture production	5	0.7	0.1—3.4
Water transport	17	0.6	0.3—1.2
Household appliances	8	0.6	0.3—1.7
Depository institutions	6	0.6	0.2—1.6
Industrial machinery	14	0.4	0.2—0.9
Ship building	14	0.5	0.3—1.0
Electric utilities	7	0.3	0.1—1.0
Retail services	15	0.4	0.2—0.8
Pharmaceutical production	6	0.4	0.1—0.9

^a Adjusted for age, smoking, and alcohol consumption.

The odds ratios for laryngeal cancer are shown in table 4 by industry. The workers in local governments (OR 4.7, 95% CI 1.7—12.5), trade unions (OR 3.6, 95% CI 1.1—11.7), and grain mills (OR 3.1, 95% CI 1.3—7.6) had elevated odds ratios. Industries showing deficits included pharmaceutical production (OR 0.4, 95% CI 0.1—0.9), retail services (OR 0.4, 95% CI 0.2—0.8), and industrial machinery production (OR 0.4, 95% CI 0.2—0.9). The risk of supraglottic cancer was elevated among the local government laborers (OR 5.9, 95% CI 1.8—19.9), and other cancers were elevated among the workers in grain mills (OR 4.9, 95% CI 1.8—13.7) (table 5).

Persons employed in the textile industries, including textile mills, yarn mills, and knitting mills had no excess risk of laryngeal cancer (OR 1.2, 95% CI 0.8—1.6). The blue-collar textile workers in the textile industries had an excess risk (OR 1.9 95% CI 1.2—3.3) (table 2), which contrasted with the findings for white-collar workers in these industries, who had no excess risk of laryngeal cancer (OR 0.4 95% CI 0.3—1.6). All the workers in the knitting mills with laryngeal cancer were blue-collar workers with clear excess risk (table 4). White-collar workers in the textile and yarn mills had no excess risk of laryngeal cancer [(OR 0.6 95% CI

Table 5. Risk of laryngeal cancer by cancer site for selected industries. (OR = odds ratio, 95%CI = 95% confidence interval)

Industry	Cases (N)	OR ^a	95% CI
Local government			
Glottis	2	2.7	0.5—13.8
Supraglottis	9	5.9	1.8—19.9
Other	4	4.0	1.0—14.5
Trade unions			
Glottis	4	4.4	1.0—19.0
Supraglottis	8	3.9	0.9—16.4
Other	3	2.5	0.6—11.5
Grain mill			
Glottis	3	2.8	0.7—11.4
Supraglottis	4	1.6	0.5—5.4
Other	7	4.9	1.8—13.7
Industrial machinery			
Glottis	1	0.1	0.0—1.1
Supraglottis	8	0.6	0.3—1.4
Other	5	0.4	0.1—1.4
Electric utilities			
Glottis	—	—	—
Supraglottis	6	0.8	0.3—2.1
Other	1	—	—
Retail			
Glottis	—	—	—
Supraglottis	10	0.7	0.3—1.4
Other	5	0.4	0.1—1.3
Pharmaceutical product			
Glottis	2	0.3	0.0—2.1
Supraglottis	1	0.1	0.0—1.0
Other	3	0.7	0.2—2.3

^a Adjusted for age, smoking, and alcohol consumption.

0.2—1.7) and (OR 0.4 95% CI 0.3—1.7) respectively], while blue-collar workers did [(OR 1.8, 95% CI 0.9—3.2) and (OR 1.7, 95% CI 1.0—4.9), respectively].

Discussion

A previous report using these data found that laryngeal cancer was significantly associated with smoking and alcohol consumption in Turkey (22), and all the analyses of risk of laryngeal cancer by occupational risk factors in this report were adjusted for tobacco and alcohol consumption, as well as age. The significant excess risk of laryngeal cancer among blue-collar workers suggests a role for occupational factors in its etiology. The risk of laryngeal cancer was elevated among guards, production supervisors, textile workers, drivers, construction workers, grain mill workers, and employees of union organizations, local government laborers, fire fighters, and street cleaners. Deficits occurred for general managers, electricians and other employees in electric utilities, pharmaceutical production workers, retail service workers, and industrial machinery production workers.

The relationship between occupation and the morphological location of laryngeal cancer has received little attention. The etiology of the different morphological regions of the larynx is not clear. We do know that the morphological distribution varies around the world. In the Mediterranean area, most cases occur in the supraglottic region (26), while glottic localization is more common in western Europe (5). In this study almost half of the cases were in the supraglottic region (46.6%). We found that the risk of supraglottic cancer was elevated among textile workers, construction workers, and local government laborers, but glottic cancers were not. These are all occupations with possible exposure to dust, which suggests that dust and particulates may be involved in the etiology of larynx cancer.

We observed an excess risk for blue-collar textile workers but not for the all workers in the textile industry. A subgroup analysis of workers in the textile industry showed that the blue-collar workers experienced an excess risk, but no excess risk was observed for the white-collar workers (managers, administrative clerks, office clerks, etc). Thus blue-collar workers in all segments of the textile industry appear to have an elevated risk of laryngeal cancer. The difference between the blue-collar and white-collar workers explains the discordant results from textile mills, yarn mills, and knitting mills. Knitting mills had the highest odds ratio, and all of its nine laryngeal cases occurred in blue-collar textile workers. No excess was observed in textile and yarn mills where there were many white-collar workers. Several other studies have noted excesses of laryngeal can-

cer among textile workers (18, 19, 27—29). We think dust exposure may play a role. Textile workers who have contact with dust, such as fabric and leather dust, have been linked with an elevated risk of laryngeal cancer earlier (13, 20, 29).

Many studies (13, 18, 30—32), but not all (33), have noted an elevated risk of laryngeal cancer among drivers, as observed in this study. Drivers in these data were mostly diesel engine truck drivers (97.3%). Further evaluation of engine exhaust is needed with respect to the development of laryngeal cancer.

The excess of laryngeal cancer we observed among construction workers may be due to exposures to organic or inorganic dusts, paint, engine exhaust, or welding fumes. Dusts (cement, metal, wood and others) are potential exposures among construction workers and may contribute to the excess of laryngeal cancer (13, 14, 27, 32, 34—36).

The excess risk among guards has not been observed in earlier studies, but elevated risk has been reported for production supervisors and various groups of service workers (31, 34). The job duties of guards in different industries are likely to be similar (ie, usually they work at night and control the security of the work area). However, an industry-based analysis showed slightly increased risks among guards in highway construction and the textile industries; this finding suggests that the industry in which guards are employed is likely to determine the exposure among guards. This result paralleled the pattern noted for production supervisors and further suggests some factor(s), possibly dust in the workplace, affecting the development of laryngeal cancer.

Results for several other occupations suggest that exposure to dust may be a risk factor for laryngeal cancer (19, 20, 28). In this study we found an excess risk for street cleaners. Street cleaning in Turkey is largely a manual operation and workers may have considerable exposure to dust during the sweeping of the streets. Workers in grain mills have considerable potential for dust exposure, although pesticide exposures are also possible in this industry (10, 20). A nearly fivefold excess of laryngeal cancer was noted among laborers in local government services. Outdoor work and dust exposure are common among these workers, who mostly work in municipal regions as laborers in urban maintenance and service occupations, such as park recreation, sidewalk construction, and excavations for underground cable or pipeline repairs.

Although there were only seven firefighters with laryngeal cancer in this study, there was nearly a fourfold excess risk. Elevated rates of laryngeal cancer have been reported in some earlier studies of firefighters (37) but not in others (38).

The deficits of laryngeal cancer among occupational groups, such as general managers, may be due to the

effect of socioeconomic status and reflect the impact of diet, income, and education. We did not have detailed information on these variables and could not directly evaluate the involvement of socioeconomic status on laryngeal cancer risk. Others have noted that occupations with a higher socioeconomic status have a lower risk of larynx cancer (39), and we observed that the risk of laryngeal cancer was greater among blue-collar workers than white-collar workers.

Pharmaceutical production workers and electricians had a decreased risk. It seems less likely that socioeconomic status plays a role in these groups. Drug production workers work in relatively "sterile" areas, but still they may have contact with chemical, physical, and biological carcinogens. Although a previous study reported an increased risk of laryngeal cancer among workers exposed to electromagnetic fields (40), electricians' work conditions are much better than many other occupations in terms of dust exposure.

Although these data provided us with a unique opportunity to evaluate the role of occupational factors in the origin of laryngeal cancer in a developing country, they have several limitations. We lacked direct information on socioeconomic status, duration of employment in each job, and actual monitoring data for occupational exposures. The lack of population-based referents could also have been a limitation, but cancer referents have been effectively used in past studies (41). Our analyses using a small alternative set of referents without cancer did not show any significant differences from the odds ratios based on cancer referents. Although we had some information on alcohol and tobacco use, the level of consumption was not available for about 50% of the subjects. Adjustments of the odds ratios by ever use of tobacco and alcohol could have left residual confounding. We actually found little difference in the odds ratios with and without such adjustment. This finding suggests either that adjustment by the ever-never use of tobacco and alcohol is completely ineffective or that odds ratios by occupation and industry are not confounded by tobacco and alcohol patterns. We do not believe there is a serious problem of residual confounding because (i) in the face of real confounding it is unlikely that ever-never adjustment would have no effect, (ii) adjustment by the level of use among the subgroup that had such information gave odds ratios nearly identical to those from the ever-never adjustment, and (iii) previous reports in the literature have found few examples of confounding of occupational cancer risks by tobacco use (42, 43).

The major strength of the study was the large number of larynx cancer cases from a developing country in which occupational exposures may be greater than in developed countries, where most previous studies on occupation and laryngeal cancer have been conducted.

In summary, in a large study in Turkey, we found elevated risk of laryngeal cancer among textile workers, drivers, construction workers, and workers among grain mills, guards, production supervisors, labor unions, and local government services. Analyses by the morphological location of the cancers suggested that supraglottic larynx cancer may be more strongly associated with occupations with possible exposure to dusts than cancers at other locations. Future studies should evaluate the relationship between occupational exposures and cancer in different morphological regions of the larynx with more detailed exposure assessment methods. An analysis of a job-exposure matrix of different chemicals, which is in process for these data, will give us a chance to evaluate further occupational factors in the etiology of lung cancer.

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Received for publication: 7 November 2000