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## BACKGROUND

Cancer of the larynx may develop in the glottis (the central part of the larynx that includes the vocal cords), the supra glottis (the area above the glottis), or more rarely in the sub glottis (the area of connection of the larynx to the trachea). It is much more commonly diagnosed in males than females and in developed countries among those aged 60 years and older.

Incidence of laryngeal cancer among males is high in some parts of South America (Argentina, Uruguay, and Cuba), in southwestern Europe (Italy, Spain, and France), in parts of Central/Eastern Europe (Croatia, Slovakia, Yugoslavia, Poland, and Belarus) and in US Blacks. In all these populations, the age-standardized incidence rate (ASR) per 100,000 in males is above 10 per annum. Among females, the highest rates are in US Blacks, but these rates do not exceed 3 [1].

The primary risk factors for laryngeal cancer are tobacco and alcohol. A careful review of several sources of epidemiological evidence concluded that there is a strong dose-response relationship between cigarette smoking and laryngeal cancer [2]. Estimates of relative risk for those reporting smoking over 20 cigarettes per day range from around 4 [3] to 30 [4]. Studies have also shown that the risk decreases with the numbers of years since smoking cessation [5,6].

The evidence that alcohol exposure causes laryngeal cancer is strong, although its quantification is more difficult to pinpoint because researchers have used different measures for exposure. Most investigators have identified a four- to five-fold risk between heavy drinkers and nondrinkers, although the definition of a heavy drinker has varied [7-11].

Many studies have shown that alcohol consumption and cigarette smoking have an independent multiplicative effect on risk. The most recent reports are those of Dosemeci et al. [11], carried out in Turkey, and Schlecht et al. [12], in Brazil. This means that a heavy smoker who also drinks heavily may have a risk 60 times that of someone who abstains from smoking and alcohol (fifteen-fold due to the smoking, multiplied by four-fold due to the alcohol). There are also some reports of synergism – in other words, higher relative risks for smoking among drinkers than among nondrinkers [10,13], but this has not been seen in other studies [14-16].

The fact that these risk behaviors are more common among males than females probably explains the approximately five-fold difference in the incidence of laryngeal cancer between men and women seen in many countries.

Poor eating habits are often associated with alcohol abuse and may be part of the reason that the incidence of laryngeal cancer is higher among heavy drinkers. In particular, low carotenoid intake, resulting from low consumption of fresh vegetables, has been associated with a greater risk of laryngeal cancer [17]. In a Phase II prevention trial, 13-cis retinoic acid was found to reduce the risk of second primary head and neck tumors [18].

Occupational exposure studies have suggested links between laryngeal cancer and exposure to asbestos or chromium [19]; however, these suggested relationships have not been confirmed.

RESULTS

Table 7.1 presents the numbers, proportions by age group, incidence rates age-standardized to the world standard, and age-specific incidence rates for MECC populations and the US SEER population.

The total numbers of cases from each population were less than 150, except for Israeli Jews, Jordanians, and the US SEER population; therefore, extensive analysis was not possible. Numbers among females were particularly low, except in Israeli Jews and US SEER. The proportion of cases in persons over 60 years of age was around two thirds in US SEER, Israeli Jews, and Cypriots, and around one half in Egyptians, Jordanians, and Israeli Arabs. These differences are largely due to differences in the population age distribution.

Unlike lung cancer, the overall ASRs for laryngeal cancer were not much lower in the MECC populations than in the US SEER population. The rate in Israeli Arab males (6.0) appeared to exceed that in US SEER males (4.6). The rate in Israeli Jews, Jordanians, and Egyptians was similar to the SEER rate. The rate in Cypriots

appeared lower than in the other MECC populations. The laryngeal cancer rates among females in MECC populations appeared to be very low, but estimates are based on such small numbers that the actual levels cannot be precisely determined. The exception is among Israeli Jewish females, who appeared to have a lower incidence rate (0.6) than that of US SEER females (1.0).

The MECC rates of laryngeal cancer in males appeared similar to that of Algeria (4.3), but higher than those reported in Kuwait (2.9) and Oman (1.6). The low MECC rates in females are similar to those in other Middle Eastern countries [1].

Given that cigarette smoking is the major risk factor for both laryngeal cancer and lung cancer, the different patterns seen in the incidence rates are puzzling. One might expect the ratios of the ASRs between 2 countries to be similar, but as mentioned above, laryngeal cancer incidence in MECC populations is similar to that of SEER, whereas lung cancer incidence rates in MECC are much lower than in SEER. This difference cannot be explained by alcohol consumption. Levels of alcohol consumption are higher in the SEER

Table 7.1. Laryngeal Cancer: Number of Cases, Age Distribution, and Age-Standardized Incidence Rates, by Age and Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001\*

	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER <sup>†</sup> 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
<b>Total cases</b>	59	53	6	886	756	130	112	103	9	145	133	12	365	335	30	3,927	3,107	820
<b>Age Groups (Distribution)</b>																		
<60 y	28.8%	30.2%	-	30.5%	30.6%	30.0%	49.1%	50.5%	33.3%	51.7%	50.4%	66.7%	46.6%	46.0%	53.3%	33.2%	32.9%	34.4%
60+ y	71.2%	69.8%	83.3%	69.5%	69.4%	70.0%	50.9%	49.5%	66.7%	48.3%	49.6%	33.3%	53.4%	54.0%	46.7%	66.8%	67.1%	65.6%
<b>Age Groups (Rates)<sup>‡</sup></b>																		
<b>Total rate</b>	1.6	3.0	0.2	2.4	4.6	0.6	3.1	6.0	0.5	2.2	4.2	0.3	2.7	4.8	0.4	2.7	4.6	1.0
<60 y	0.6	1.1	-	1.0	1.9	0.3	1.5	2.7	0.2	1.1	2.0	0.2	1.2	2.0	0.2	1.0	1.7	0.4
60+ y	9.5	18.7	1.6	13.7	26.9	3.4	16.5	32.0	3.3	11.3	22.2	1.3	15.1	27.4	2.2	15.8	28.3	5.8

\*The symbols "-" = 1-2 cases; and "[numeral]" (italic) = 0 or 3-15 cases.

†SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

‡Rates are per 100,000 and are age-standardized to the World Standard Million.

**Table 7.2. Laryngeal and Lung Cancer: Age Distribution of Cases among US SEER\* Males --1999-2001†**

	Laryngeal Cancer 1999-2001	Lung Cancer 1999-2001
<b>Total cases</b>	3,107	34,973
<35 y	0.2%	0.2%
35-39 y	0.7%	0.5%
40-44 y	2.7%	1.6%
45-49 y	5.7%	3.1%
50-54 y	10.5%	5.9%
55-59 y	12.9%	9.0%
60-64 y	15.2%	12.6%
65-69 y	15.7%	15.1%
70-74 y	15.1%	18.5%
75+ y	21.1%	33.4%

\*SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

† [Numerals] (italic) = 0 or 3-15 cases.

populations than in MECC, so one might expect an even larger difference between MECC and SEER in laryngeal cancer incidence than in lung cancer incidence – the opposite of the pattern observed.

Table 7.2 shows a comparison of the percentage of lung cancer cases and laryngeal cancer cases by age among males in the US SEER population. This shows that laryngeal cancer tends to develop at an earlier age than lung cancer. Other data show the same trend. One may therefore infer that the latent period to laryngeal cancer after smoking begins is shorter than for lung cancer. This being the case, the similarity of laryngeal cancer rates in MECC and SEER could be hypothesized to be due to the similarity in more recent years of the smoking prevalence in these populations (for example, see Figure 6.1). Conversely, lung cancer rates could be hypothesized to be different due to higher smoking prevalence in the SEER population in a period previous to that shown in Figure 6.1.

However, this hypothesis does not seem to hold on examination of the age-specific rates of laryngeal cancer in Israeli Jewish and

US SEER males, by 5-year age groups (Table 7.3). If the above hypothesis were true, one would expect to see Israeli rates somewhat higher at younger ages and somewhat lower at older ages. Instead, one sees that rates are similar at all ages.

The great majority of registered cases of laryngeal cancers are microscopically confirmed. In the US SEER population, Cyprus, and Jordan, the percentage is over 98%. In Egypt and Israel, it is around 90% (see Table 1.2). Differences in microscopic confirmation rates between the registries are discussed in Chapter 1.

### SUMMARY AND CONCLUSIONS

The incidence of laryngeal cancer in males in the MECC populations was comparable to that in US SEER, except that it appeared somewhat higher in Israeli Arabs and somewhat lower in Cypriots. One might expect that the MECC rates should be lower than in the US SEER population, similar to lung cancer, but this was not the case. Further investigation of the reasons seems indicated.

**Table 7.3. Laryngeal and Lung Cancer: Age-Standardized and Age-Specific Incidence Rates\* among Israeli Jewish and US SEER Males – 1996-2001**

	Laryngeal Cancer Israel (Jews) 1996-2001	Laryngeal Cancer US SEER† 1999-2001	Lung Cancer Israel (Jews) 1996-2001	Lung Cancer US SEER† 1999-2001
<b>Total rate</b>	4.6	4.6	28.4	48.6
40-44 y	2.2	1.8	9.9	11.6
45-49 y	4.5	4.3	20.2	26.6
50-54 y	11.5	9.2	35.8	58.7
55-59 y	15.3	15.4	79.2	120.7
60-64 y	23.0	24.1	137.6	225.4
65-69 y	27.6	30.7	202.6	332.1
70-74 y	32.1	33.5	242.9	461.0
75+ y	28.5	27.8	236.8	498.9

\*Rates are per 100,000 where appropriate, and are age-standardized to the World Standard Million.

†SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

Since cigarette smoking is the major known risk factor for laryngeal cancer, and alcohol consumption in the MECC populations is generally low, monitoring of smoking prevalence combined with programs for smoking cessation would be expected to help reduce the incidence of laryngeal cancer in MECC countries.

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