ASBESTOS, DENTAL X-RAYS, TOBACCO, AND ALCOHOL IN THE EPIDEMIOLOGY OF LARYNGEAL CANCER

M. WARD HINDS, MD, MPH,*† DAVID B. THOMAS, MD, DR PH,‡ AND H. P. O'REILLY, MPH*

A case-control study of 47 laryngeal cancers in males of three counties of Washington State was conducted. Personal interview was used to obtain information on smoking, alcohol use, exposure to asbestos, and other substances, and x-rays of the head and neck area. Smoking and alcohol consumption were found to increase risk of laryngeal cancer independently, with a clear dose-response relationship. Neither asbestos exposure nor exposure to other substances was found to significantly increase the risk of laryngeal cancer, although the relative risk with asbestos exposure was 1.75. Lifetime history of exposure to dental x-rays on five or more occasions was associated with significantly increased risk of laryngeal cancer among heavy smokers but not among light smokers. The importance of tobacco and alcohol in the epidemiology of laryngeal cancer was re-affirmed, the importance of asbestos exposure was brought into question, and a possible relationship of laryngeal cancer with exposure to dental x-rays among heavy smokers was demonstrated.

Cancer 44:1114–1120, 1979.

CERTAIN RISK FACTORS for cancer of the larynx have been well established by epidemiologic studies. These include smoking, alcohol, and male sex.[9,11,16,20,21] In addition, various occupational exposures have been investigated as possible causes of cancer of the larynx. Chemical exposures have been implicated by two studies. Cancer mortality was examined among 139 U. S. counties with the highest proportion of employment in the chemical industry.[7] It was found that these chemical industry counties showed a statistically significant 10% elevation in mortality from cancer of the larynx when compared to total U. S. mortality. A case-control study carried out at the Roswell Park Memorial Institute found significantly elevated relative risk for laryngeal cancer among barbers, operatives in the chemical industry, and operatives in the leather industry.[19] Smoking history but not alcohol intake was controlled for in the analysis. A mortality study of male workers in a nickel refinery disclosed 5 laryngeal cancer deaths when only 1.4 deaths were expected based on national mortality rates in Norway.[13] An association of laryngeal cancer with wood dust exposure among nonsmokers but not among smokers has also been noted.[21]

Considerable interest has been aroused concerning the possible association of asbestos exposure and risk of laryngeal cancer. Asbestos is known to be associated with bronchogenic carcinoma and mesothelioma and possibly other cancers.[1] In 1973, Stell and McGill reported a case-control study of 100 males with laryngeal cancer.[17] They found that 31 cases reported exposure to asbestos as compared to only 3 controls for a relative risk (RR) of 14.5. The same year a brief report on a cohort of workers at an asbestos textile and cement factory indicated that 2 deaths from cancer of the larynx had occurred, whereas only 0.37 were expected.[12] A second case-control study in 1975 found that 10 of 43 males with laryngeal cancer gave histories of exposure to asbestos compared with none of the age-matched neighborhood controls.[15]

The present study was initiated following an investigation of mesothelioma incidence in

From the *Occupational Health Section, Washington State Department of Social and Health Services, Olympia, Washington, †Cancer Center of Hawaii, Epidemiology Program, University of Hawaii, Honolulu, Hawaii, ‡Fred Hutchinson Cancer Research Center, Seattle, Washington

Supported in part by NCI Grant No. NCI/CA 1574 and Contract NOI-CP-53511.

Address for reprints: Dr. M. W. Hinds, Cancer Center of Hawaii, University of Hawaii, 1236 Lauhala, Suite 407, Honolulu, HI 96813.

Accepted for publication September 18, 1978.

0008–543X/79/0900/1114 $0.85

the area of Puget Sound, Washington State, where there is considerable shipbuilding activity and, thus, asbestos use.[6] Because mesothelioma incidence was found to be significantly and greatly elevated in the one county that contains a very large Naval shipyard, incidence rates for cancer of the larynx were also examined for that county. Surprisingly, that county was found to have the lowest, rather than the highest, age-adjusted incidence of laryngeal cancer in men of the six counties examined. There was no correlation between incidence of mesothelioma and incidence of laryngeal cancer by county (Table 1). The question was thus raised of whether asbestos exposure is related to risk of laryngeal cancer in the Puget Sound area. This study was designed to explore that question and to examine other exposures which might have a relationship to risk of laryngeal cancer.

TABLE 1. Incidence of Mesothelioma and Laryngeal Cancer in Six Washington Counties, 1974–76

County	Average annual age-adjusted incidence per 100,000 males	
	Laryngeal cancer (N = 220)	Mesothelioma (N = 34)
Pierce	10.0	0.9
Greys Harbor	8.6	0.9
Thurston	8.0	0.8
King	6.8	1.0
Snohomish	5.5	0.8
Kitsap	4.0	4.5

MATERIALS AND METHODS

All males diagnosed as having laryngeal cancer while residents of Pierce, King, or Kitsap counties between January 1, 1976 and June 30, 1977 were identified through the Cancer Surveillance System (CSS) of the Fred Hutchinson Cancer Research Center in Seattle. The CSS is a population-based cancer registry and a member of the Surveillance, Epidemiology and End Results (SEER) Group of the National Cancer Institute. Sixty-nine such cases were identified and 47 of these were included in this study. The remaining 22 cases were excluded because their private physicians were unwilling for their patients to be interviewed (10), the patient was deceased with no close relatives (8), the patient could not be located (2) or the patient refused to be interviewed (2).

A neighborhood control was chosen for each case with matching for sex, race, and 10-year age group. Controls were chosen by a door-to-door survey starting at the third house to the right of the case's address and following a written set of directions until a control was found. A potential control address was not to be abandoned until at least two visits at different times of the day and two phone calls, one at night, were unsuccessful. No addresses had to be abandoned with this procedure, although 8 potential controls refused to be interviewed and were replaced by others in the same neighborhood.

All cases and controls read and signed an informed consent form and received a copy prior to being interviewed. The interviews were carried out by two of the authors (MWH and HPO) with matched cases and controls always interviewed by the same person. Interviews were conducted either in the subject's home or at his place of work. In three instances where the case was deceased, a primary relative (wife, brother) who lived with the deceased for many years was interviewed. The same relative of the matched control for these cases was interviewed rather than the control himself. The interviewer employed a standard questionnaire and over a period of 20 to 30 minutes elicited a detailed history of places and nature of employment throughout the subject's life and specific histories of

TABLE 2. Comparison of Usual Cigarette Consumption Levels for Cases and Controls

Cigarettes per day	Cases		Controls			
	Percent	(No.)	Percent	(No.)	RR*	p
Less than 10	4.2	(2)	34.0	(16)	1.00	
10–20	27.7	(13)	29.8	(14)	7.13	<.025
21–40	46.8	(22)	27.7	(13)	13.54	<.01
More than 40	21.3	(10)	8.5	(4)	20.00	<.01
TOTAL	100.0	(47)	100.0	(47)		

Test for trend, $p < .001$.

* Risks are expressed relative to a risk of 1.00 for consumption of less than 10 cigarettes per day.

TABLE 3. Comparison of Total Pack-Years of Cigarette Exposure for Cases and Controls

Pack-years exposure	Cases		Controls			
	Percent	(No.)	Percent	(No.)	RR*	p
Less than 10	4.3	(2)	34.1	(16)	1.00	
10–39	25.5	(12)	31.9	(15)	6.40	<.05
40–69	40.4	(19)	17.0	(8)	19.00	<.001
70 or more	29.8	(14)	17.0	(8)	14.00	<.01
TOTAL	100.0	(47)	100.0	(47)		

Test for trend, $p < .005$.

* Risks are expressed relative to a risk of 1.00 for exposure to less than 10 pack-years.

exposure to asbestos, arsenic, nickel, uranium, chromium, cobalt, and other chemicals or materials felt to be of importance to the subject. In addition, a detailed smoking history, alcohol consumption history, history of x-ray exposure in the head and neck area, and history of hobbies were obtained.

All cases were classified according to site of origin of the tumor (glottic, supraglottic, other) and all data were coded and keypunched for analysis.

For 2 × 2 matched-pair tables with small cell frequencies, the method suggested by Bennett and Underwood was used for testing significance.[2] Chi-square analysis was used where matching was not maintained.

RESULTS

All 47 laryngeal cancers were in Caucasians. There was no significant difference between the mean age at diagnosis of the cases (63.0 ± 8.3*) and the controls (63.1 ± 9.2), indicating that matching on age was successful. In addition there was no significant difference between the mean age of the cases and the mean age of all male laryngeal cancer cases identified by CSS in the three counties under study for the period January 1, 1975 through June 30, 1977 (63.2 ± 9.2, N = 153). A comparison of the 47 study cases to these same 153 total cases likewise revealed no significant difference for site of tumor, county of residence, or marital status. Thus, the study population of 47 cases would appear to be representative of all laryngeal cancer cases occurring in males during this period and in this geographic area.

The site of the cancer was glottic for 35 of the cases (74.5%), supraglottic for 9 (19.1%), and subglottic or other for the remaining 3 cases. This is a higher proportion of glottic cases than has been reported in a study by Wynder *et al.*[21] but may reflect the substantial population of Swedish ancestry in the Puget Sound area, since glottic cancers in Sweden may constitute up to 89% of all laryngeal cancer.[10] In the 1970 census, the three counties surveyed in this study had a proportionate Swedish population more than four times greater than Wynder's population.[18]

A comparison of the 47 cases interviewed with the 22 cases not interviewed revealed that the cases not interviewed were slightly younger (60.7 ± 7.5 years), less likely to be married (77.3% versus 80.9%), and less likely to have a glottic cancer (54.5% versus 74.5%), but none of the differences were statistically significant.

* Mean ± standard deviation.

TABLE 4. Comparison of Usual Level of Alcohol Consumption for Cases and Controls

Alcohol per day	Cases		Controls			
	Percent	(No.)	Percent	(No.)	RR*	p
Less than 1 unit	23.4	(11)	53.2	(25)	1.00	
1–2 units	19.2	(9)	21.2	(10)	2.05	N.S.
3–6 units	31.9	(15)	19.2	(9)	3.79	<.05
More than 6 units	25.5	(12)	6.4	(3)	9.01	<.01
TOTAL	100.0	(47)	100.0	(47)		

Test for trend, $p < .001$.

* Risks are expressed relative to a risk of 1.00 for consumption of less than 1 unit per day.

The relationship of smoking and alcohol consumption to risk of laryngeal cancer were analyzed without maintaining matched pairs. The smoking association, with a dose-response relationship, was apparent whether one examined the usual level of cigarette consumption (Table 2) or the total pack-years consumption calculated from the year of starting smoking to the year of diagnosis for the case (Table 3). Exsmokers were combined with current smokers for all analyses. Only 1 of the cases but 8 of the controls were nonsmokers. Usual alcohol consumption was calculated on the basis of units per day, with the approximation that one unit = 1 ounce of hard liquor = 4 ounces of wine = 12 ounces of beer. The results in Table 4 clearly demonstrate an association between alcohol consumption and risk of laryngeal cancer and strongly suggest a dose-response relationship.

Although the number of cases was small, it was possible to demonstrate that smoking and alcohol consumption appear to act as independent risk factors (Table 5). This would agree with the findings of previous studies.[21] Although synergism was suggested,[3] the broad, open-ended categories do not really allow such analysis.

For a history of exposure to asbestos, 25 (53.2%) of the cases and 19 (40.4%) of the controls gave a positive response. There were 14 matched pairs for which only the case was exposed to asbestos and 8 pairs for which only the control was exposed. Matched pair analysis of asbestos exposure thus gave a RR for laryngeal cancer of 1.75, which was not statistically significant. When the duration of exposure to asbestos was examined for cases and controls with an exposure history, again there was no significant difference (8.4 ± 8.2 years and 8.3 ± 7.5 years, respectively), and no dose-response effect could be demonstrated. The sources of asbestos exposure (shipyards, brake repair, construction) were also similar for both cases and controls. A lack of significant association between asbestos exposure and laryngeal cancer was found for both glottic and supraglottic cases, and for case-control pairs fortuitously matched for smoking and alcohol consumption (Table 6). The RR was consistently greater than 1.00 for each category of pairs analyzed, however.

Very few cases or controls gave a history of exposure to arsenic, nickel, uranium, chromium, or cobalt and there was no significant association found between exposure to any one of these and risk of laryngeal cancer.

TABLE 5. Relative Risks of Laryngeal Cancer According to Presence or Absence of Two Exposures—Heavy Drinking and Heavy Smoking*

		Heavy smoking	
		No	Yes
Heavy drinking	No	1.00†	2.14
	Yes	2.25	8.10

* Heavy drinking is defined as one or more units of alcohol per day; heavy smoking as more than 20 cigarettes per day.

† Risks are expressed relative to a risk of 1.00 for persons who are neither heavy drinkers nor heavy smokers.

There was some suggestion of an association between a history of exposure to dental x-rays and risk of laryngeal cancer. Cases and controls were asked to estimate the number of times in their lives that a visit to a dentist had involved dental x-rays. Cases reported a mean of 14.3 dental x-ray visits and controls a mean of 12.3, a nonsignificant difference. The frequency distribution of the number of dental x-ray visits was highly skewed however, with 15 (31.9%) cases and 22 (46.8%) controls giving a history of only 0–4 dental x-ray visits. Because of a concern about the possibility of confounding of any association of dental x-rays and laryngeal cancer by either smoking or alcohol use, the relationships between smoking and dental x-rays and between alcohol use and dental x-rays were examined for all 94 subjects. No statistically significant association could be found in any analysis of number of dental x-ray visits versus number

TABLE 6. Matched-Pair Analysis of Asbestos Exposure in Relation to Risk of Laryngeal Cancer

Pairs analyzed	N	Pairs w/only cases exposed	Pairs w/only controls exposed	RR	p
All	47	14	8	1.75	.21
Glottic cancer	35	9	7	1.29	.63
Supraglottic cancer	9	4	1	4.00	.22
Smoking-matched*	12	3	1	3.00	.37
Alcohol matched†	12	4	3	1.33	.73

* Matched on smoking categories in Table 2.

† Matched on alcohol consumption categories in Table 4.

TABLE 7. Comparison of Number of Dental X-ray Visits by Cases and by Controls Among Smokers of 21 or More Cigarettes a Day

No. of dental x-ray visits	Cases		Controls			
	Percent	(No.)	Percent	(No.)	RR*	p
0–4	21.9	(7)	64.7	(11)	1.0	
5–9	18.8	(6)	11.8	(2)	4.7	N.S.
10 or more	59.3	(19)	23.5	(4)	7.5	<.02
TOTAL	100.0	(32)	100.0	(17)		

Test for trend, $p < .005$.

* Risks are expressed relative to a risk of 1.0 for exposure to less than 5 dental x-ray visits.

of cigarettes a day smoked or number of units of alcohol a week consumed. Specifically, there was no evidence that more heavy smokers were present among the groups with more dental x-ray visits. For the categories of 0–4, 5–9, and 10 or more dental x-ray visits, the percentage of heavy (21+/day) smokers was 48.6, 44.4, and 56.4, respectively. The dental x-ray data were then analyzed in two ways to determine association with laryngeal cancer risk. First, the matching of pairs was disregarded and evidence of a dose-response was sought. Among light smokers (20 or fewer cigarettes per day), there was no increased risk of laryngeal cancer found in association with dental x-ray visits. However, among heavy smokers, a dose-response relationship was suggested and a significant relative risk of 7.5 was found when a history of 10 or more dental x-ray visits was reported (Table 7). A matched pair analysis revealed 12 case-control pairs in which only the case was exposed to five or more dental x-ray visits versus 5 pairs in which only the control was so exposed. This difference was not significant, but when the matched pair analysis was stratified by smoking level, a significant association was found among heavy smokers (21 or more cigarettes per day) between exposure to 5 or more dental x-ray visits and laryngeal cancer (Table 8). No association was found between laryngeal cancer and other x-rays of the head and neck, but the number of persons giving such an exposure history was too small for meaningful analysis.

DISCUSSION

This study found, as have others, that the most readily identifiable risk factors for laryngeal cancer are tobacco and alcohol consumption.[9,20,21] The findings in this study, however, are not supportive of the hypothesis that asbestos exposure is an important risk factor for cancer of the larynx, although the RR of 1.75 found is consistent with a small risk associated with asbestos exposure. Both the studies of Stell and McGill[17] and Shettigara and Morgan[15] found very high relative risks for laryngeal cancer associated with asbestos exposure (RR = 14.5 and ∞, respectively). It is difficult to understand why such a strong relationship would have been missed in the current study if it is a real one. The investigation of Stell and McGill used hospital controls with no apparent matching other than sex and age. No alcohol consumption history was taken. We do not know if both cases and controls were interviewed by the same individual using a standardized format. Some possibilities for bias thus exist, but it is difficult to see how such biases would produce a RR of 14.5. One question which needs to be answered is whether the laryngeal cancer

TABLE 8. Comparison of Matched Case-Control Pairs for Exposure to Dental X-rays

	N	Pairs w/only cases exposed*	Pairs w/only controls exposed	RR	p
All matched pairs	47	12	5	2.40	.10
Pairs matched for smoking†					
Light	10	2	2	1.00	1.00
Heavy	12	5	0	∞	.04

* Exposed = 5 or more dental visits with x-rays taken.

† Light smoking = 20 or fewer cigarettes per day; heavy smoking = 21 or more cigarettes per day.

cases were likely to gain any workmen's compensation benefits by linking a past working exposure to their illness. Such a situation could indeed introduce a large bias if the nature of the investigation was at all apparent to the cases prior to or during the interview.

The investigation by Shettigara and Morgan did match on neighborhood of residence as well as sex and age, thus using a control group very similar to that of the current study. Four of the cases were apparently interviewed by clinic personnel while all the controls and the remainder of the cases were interviewed in their homes by a single interviewer. It seems possible that a search for asbestos exposure might have been somewhat more emphasized for the 4 cases interviewed in the clinic, thus introducing some bias into the study. It is surprising that alcohol consumption was not found to be related to risk of laryngeal cancer even though this is apparently a well-established risk factor.[11,20,21] Asbestos-exposed cases were more often smokers than non-asbestos exposed cases (100% versus 90.9%) although the difference was not significant. Again, although some potential for bias can be shown, it is difficult to see how bias alone might produce the high RR found for asbestos exposure.

The primary difference in the findings of the present study as compared to the two above was in the proportion of controls who were found to give a positive history for asbestos exposure. Only 3% of the controls of Stell and McGill and none of the controls of Shettigara and Morgan reported asbestos exposure as compared to 40.4% so doing in the present study. We included any person in the asbestos-exposure category if he answered positively to an inquiry about exposure as a result of working directly with or in the vicinity of asbestos dust. It is possible that definitions of exposure used by the two previous studies were more restrictive and this is in part responsible for the different findings, or it may be that asbestos exposure in the general population is more common in the Puget Sound area of Washington State than in Liverpool or Toronto. While this might not be unexpected for Toronto, it would be somewhat surprising for Liverpool, which is in an area where mesothelioma due to asbestos exposure is not uncommon.[5] In the Puget Sound area, the shipbuilding industry was found to be a common source of occupational exposure to asbestos, with 12 of the 44 asbestos-exposed subjects identifying a shipyard job as the site of asbestos contact. However, occupational exposures also occurred frequently in construction of buildings and homes, brake lining repair, and the plumbing industry.

At least three previous studies present evidence which is not in favor of a relationship between asbestos exposure and laryngeal cancer. Selikoff *et al.* have been following three large cohorts of asbestos workers for several years and as yet no significant excess of laryngeal cancer has been observed.[14] Admittedly, laryngeal cancer is an uncommon neoplasm, but not so rare as mesothelioma for which excess mortality has been easily demonstrated in these cohorts. The case-control study of 314 cases of laryngeal cancer by Wynder *et al.* was unable to detect any occupational exposure, other than possibly wood dust in nonsmokers, which conferred excess risk of laryngeal cancer.[21] Asbestos exposure was specifically questioned for and none of the 13 nonsmoking cases were aware of such exposure. Finally, a retrospective survey of over 14,000 cancer cases admitted to Roswell Park Memorial Institute in Buffalo was carried out with comparison to nonneoplastic controls.[8] Each person was classified into as many different occupational groups as were present in the history. After adjustment for smoking history, there were no occupations usually associated with asbestos exposure which showed an increased risk for laryngeal cancer.

In summary, the relationship of asbestos exposure to laryngeal cancer appears to be open to question. A recommendation for further studies may not be warranted, however, since asbestos exposure is already coming under strict control because of its clear relationship to mesothelioma and lung cancer.[1]

The finding in the present study of a possible relationship between exposure to dental x-rays and laryngeal cancer among heavy smokers is one which does call for further investigation because of the common use of dental x-rays. Of course this relationship was based on a small number of cases and may not be real, or if real may not indicate that dental x-rays themselves are responsible for excess laryngeal cancer among heavy smokers. The frequency of visits to the dentist's office and the use of dental x-rays are undoubtedly correlated with many variables, particularly

dietary habits, which were not controlled for in this study. Also arguing against a causal association between dental x-rays and laryngeal cancer is the fact that although thyroid cancer has been found in excess among persons who have received large doses of external irradiation to the head and neck, there is as yet no evidence that these persons have an increased risk of laryngeal cancer.[4] It will require much larger studies and more detailed interviews to determine if dental x-ray exposure poses a cancer risk for heavy smokers.

ADDENDUM

After acceptance of the manuscript for publication, an additional case-control study of laryngeal cancer and asbestos exposure appeared in the literature.[22] This study was conducted in the province of Trieste, Italy, where 60 laryngeal cancer patients and 60 age- and sex-matched hospital controls were interviewed concerning smoking habits and occupational exposure to asbestos. Fifty percent of cases and 35% of controls gave a history of occupational exposure to asbestos. The relative risk of 1.86 was not statistically significant.

REFERENCES

1. Becklake, M. R.: Asbestos-related diseases of the lung and other organs: Their epidemiology and implications for clinical practice. *Am. Rev. Respir. Dis.* 114: 187–227, 1976.
2. Bennett, B. M., and Underwood, R. E.: On McNemar's test for the 2 × 2 table and its power function. *Biometrics* 26:339–343, 1970.
3. Cole, P., and MacMahon, B.: Attributable risk percent in case-control studies. *Br. J. Prev. Soc. Med.* 25: 242–244, 1971.
4. Favus, M. J., Schneider, A. B., et al: Thyroid cancer occurring as a late consequence of head and neck irradiation. *N. Engl. J. Med.* 294:1019–1925, 1976.
5. Greenberg, M., and Lloyd Davies, T. A.: Mesothelioma register 1967–68. *Br. J. Indust. Med.* 31:91–104, 1974.
6. Hinds, M. W.: Mesothelioma in the United States: Incidence in the 1970's. *J. Occupation. Med.* 20:469–471, 1978.
7. Hoover, R., and Fraumeni, J. F.: Cancer mortality in U. S. counties with chemical industries. *Environ. Res.* 9:196–207, 1975.
8. Houten, L., Bross, I. D. J., and Viadana, E.: A Retrospective Survey of Cancer in Relation to Occupation. DHEW (NIOSH) Publication 77–178, Washington, D. C., U. S. Govt. Printing Office, 1977.
9. Kahn, H. A.: The Dorn study of smoking and mortality among U. S. veterans: Report on eight and one-half years of observation. *Natl. Cancer Inst. Monogr.* 19:1–40, 1966.
10. Martensson, B.: Epidemiological aspects of laryngeal carcinoma in Scandanavia. *Laryngoscope* 85:1185–1189, 1975.
11. Monson, R. R., and Lyon, J. L.: Proportional mortality among alcoholics. *Cancer* 36:1077–1079, 1975.
12. Newhouse, M. L., and Berry, G.: Asbestos and laryngeal carcinoma. *Lancet* 2:615, 1973.
13. Pederson, E., Hogetveit, A. C., and Andersen, A.: Cancer of the respiratory organs among workers at a nickel refinery in Norway. *Int. J. Cancer* 12:32–41, 1973.
14. Selikoff, I. J., Hammond, E. C., and Seidman, H.: Cancer risk in insulation workers in the United States. *in* Biological Effects of Asbestos, P. Bogovski, et al., Eds. Lyon, International Agency for Research on Cancer, 1973; pp. 209–216.
15. Shettigara, P. T., and Morgan, R. W.: Asbestos, smoking and laryngeal carcinoma. *Arch. Environ. Health* 30:517–519, 1975.
16. Stell, P. M.: Smoking and laryngeal carcinoma. *Lancet* 1:617–618, 1972.
17. Stell, P. M., and McGill, T.: Asbestos and laryngeal carcinoma. *Lancet* 2:416–417, 1973.
18. U. S. Bureau of the Census, Census of the Population—1970. Washington, D. C., U. S. Govt. Printing Office, 1973.
19. Viadana, E., Bross, I. J., and Houten, L.: Cancer experience of men exposed to inhalation of chemicals or to combustion products. *J. Occupation. Med.* 18: 787–792, 1976.
20. Vincent, R. G., and Marchetta, F.: The relationship of the use of tobacco and alcohol to cancer of the oral cavity, pharynx or larynx. *Am. J. Surg.* 106:501–505, 1963.
21. Wynder, E. L., Covey, L. S., Mabuchi, K., and Mushinski, M.: Environmental factors in cancer of the larynx. *Cancer* 38:1591–1601, 1976.
22. Bianchi, C., Di Bonito, L., Castelli, M., and Brollo, A.: Exposition a l'amiante dans le cancer du larynx. *Pathologica* 70:403–408, 1978.