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Occupational causes of laryngeal cancer

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SUMMARY In a case-control study of all new cases of laryngeal cancer in Denmark from 1980 to 1982, 326 cases and 1134 community selected controls participated. Questionnaires were used to obtain information on education, occupation, and number of occupational exposures as well as smoking and drinking habits. High risk ratios for laryngeal cancer were found for semiskilled and unskilled workers, workers exposed to dust, out of doors workers, drivers, and people working in the cement industries and port services. The study hypothesis was that exposure to chromium or nickel increases the incidence rate of laryngeal cancer. No support for this was found concerning chromium, but exposure to nickel had a statistically significant risk ratio of 1·7.

Published reports suggest that laryngeal cancers sometimes have an occupational aetiology. Several authors have reported an increased risk for laryngeal cancer among workers exposed to asbestos,[1-7] although negative findings have also been reported.[8] It seems unlikely that this association is entirely due to confounding by alcohol and tobacco consumption, even though only few studies controlled for both of these well established risk factors.[9] One author has hypothesised that the association is confounded by chronic vocal strain, which might be associated with a noisy work environment.[10]

The risk of laryngeal cancer has also been higher than expected among workers exposed to diethyl sulphate,[11] mustard gasworkers,[12] workers at a nickel refinery in Norway,[13] painters in Sweden,[14] and in the US workers in the railroad and lumber industry, sheetmetal workers, grinding wheel operators, and automobile mechanics.[15] Since the Danish annual age standardised incidence of laryngeal cancer is 6·0 per 100 000 men compared with 1·0 for women,[16] occupational exposure may be expected to contribute to the aetiology of the disease. For this reason, we report in this paper risk ratios for laryngeal cancer according to employment and selected occupational exposures. The a priori hypothesis was that exposure to welding fumes, or other potential exposures to chromium and nickel, increases the risk of laryngeal cancer.[17 18]

Materials and methods

The study was conducted as a case-controlled study. From March 1980 to March 1982 all patients in Denmark with newly diagnosed laryngeal cancer who were under 75 at the time of diagnosis were selected as cases. The patients with cancer were ascertained from the five departments of oncology in Denmark because patients with laryngeal cancer are referred to these departments. For each case four controls were identified using the municipal person-registry in which the case was listed. Controls were matched to cases according to sex and closest possible birth date. Occasionally only three controls were sampled to match a patient with cancer. Sometimes it was not possible to find four controls born the same year as the patient or one of the controls had died recently, and was not registered as such in the local registry.

Both cases and controls received a questionnaire that included questions about exposure to a number of specific chemicals and physical agents as well as use of tobacco and alcohol. Cases and controls were asked to report their present or latest occupation and to give a description of the workplace and the type of work they performed there. Similar questions were asked about the longest held occupation. Detailed questions were asked about a number of occupational exposures such as: had they ever worked with the chemical product, when did the work take place, and for how many hours a week. Questions were asked about the degree of vocational training, the present or latest job position, and cases and controls were asked to describe their longest held occupation in a set of questions presented in a closed form. Nurses collaborating with the project abstracted the clinical information from the medical records of cases.

If necessary the controls were contacted up to three times in an effort to enlist their cooperation. Questionnaires with missing data were returned or the person was interviewed by phone. Several cases and controls, mainly the older ones, had to be interviewed. Information on alcohol use was obtained for 95% of the participating cases and 91% of the controls. Information on smoking was missing for 2% of the cases and 3% of the controls.

Information on occupation was missing for less than 2% and information on the occupational exposures for less than 6%.

Fifteen out of 375 cases (4%) and 328 out of 1462 controls (22%) refused to participate in the study. Refusals were equally distributed according to sex. In the control group the non-respondent rate was higher in the rural districts (24%) compared with the Copenhagen area (17%) and was highest among the elderly.

The site of origin of laryngeal cancer was distributed as follows: in 191 cases the cancer originated from the glottis, in 111 from the supraglottis area, in 12 from the subglottis area, and in 12 the site of origin could not be classified (326 cases). In 91% of cases the cancer was of the squamous cell type. Excluded from the case group are 32 cases in which the cancer originated from the hypopharynx and two oropharyngeal cancers.

The occupational titles were grouped according to a modified Danish version of the International Standard Classification of Occupations (ISCO 1968)[19] and the industries according to a Danish version of the International Standard Industrial Classification (ISIC 1968)[20] and an abbreviated industrial classification worked out by the Danish Work Inspectorate.[21]

Odds ratios are used as estimators of risk ratios, and adjusted values were worked out by means of the logistic regression model.[22] "Exact confidence limits" are given for the unadjusted risk ratios.[23] In the logistic regression model tobacco is included according to average daily consumption (0 g, 1–9 g, 10–19 g, and, ≥20 g), alcohol according to average daily intake (0–9 g, 10–19 g, 20–29 g, and, ≥30g). Age is entered in years at the time of selection for the study. All analyses were carried out as unmatched analyses.

Results

Table 1 shows the risk ratios for laryngeal cancer according to vocational training. The risk was highest in people with little or no vocational training and without a higher school education. Men who worked as unskilled or semiskilled workers immediately before the diagnosis or before retirement carried a risk almost twice that of professionals or salaried workers after adjustment for smoking and drinking habits (table 2).

Cases and controls were asked if they ever had worked with a number of chemicals, and when and for how long the work took place. Chromium or nickel containing chemicals were selected for this list, which also included several other widely used potential occupational hazards. Table 3 shows that only exposure to any occupational dust was statistically significantly associated with laryngeal cancer at the 5% level. Exposure to asbestos gave a

Table 1 *Risk ratios for cancer of the larynx by occupational training compared with people with an intermediate or academic degree*

Occupational training	*Sex*	*No of cases*	*Controls*	*Risk ratio**		*95% Confidence limit for adjusted risk ratio*
				Unadjusted	*Adjusted*	
Intermediate or academic degree	M	21	140	1·0	1·0	
	F	1	15	1·0	—	
Skilled	M	126	424	2·0	2·3	1·4–3·8
	F	19	39	7·3		
Semiskilled	M	44	125	2·3	2·4	1·3–4·1
	F	3	12	3·8		
None	M	77	236	2·2	2·3	1·4–3·8
	F	26	89	4·4		
Not classified	M	0	8			
	F	0	2			
Unknown	M	8	38			
	F	1	6			
Total	M	276	971			
	F	50	163			
	Both	326	1134			

*Adjusted for sex, age, tobacco, and alcohol consumption.

Table 2 *Risk ratios for cancer of the larynx according to social class compared with professionals and managers. Latest social class recorded*

Occupational training	*Sex*	*No of cases*	*Controls*	*Risk ratio**		*95% Confidence limit for adjusted risk ratio*
				Unadjusted	*Adjusted*	
Professionals and managers	M	65	227	1·0	1·0	
	F	4	5	1·0	—	
Salaried workers	M	57	298	0·8	0·7	0·4–0·9
	F	6	34	0·2		
Skilled workers	M	49	134	1·3	1·3	0·8–1·9
	F	8	13	0·8		
Semiskilled/unskilled worker	M	92	169	1·9	1·8	1·3–2·6
	F	13	16	1·0		
Not classified	M	2	31	0·2	0·4	0·2–0·7
	F	13	73	0·2		
Unknown	M	11	112			
	F	6	22			
Total	M	276	971			
	F	50	163			
	Both	326	1134			

*Adjusted for sex, age, tobacco, and alcohol consumption.

Table 3 *Relative risks for cancer of the larynx according to occupational exposures*

Exposure	*Sex*	*No of subjects*		*Risk ratios**		*95% Confidence limit for adjusted risk ratio*
		Cases	*Controls*	*Unadjusted*	*Adjusted*	
Cement	M	42	148	1·0	0·9	0·6–1·3
Antirust chemicals	M	25	62	1·5	1·5	0·9–2·4
Wood stain	M	18	67	0·9	1·0	0·5–1·6
	F	0	3			
Chromium plating	M	2	12	0·6	1·1	0·3–3·6
	F	0	2			
Textile dyes	M	4	12	1·2	1·0	0·4–2·9
	F	2	3	2·2		
Tanning material	M	1	4	0·9	1·3	0·1–11·8
Alloys	M	21	70	1·1	1·2	0·8–2·0
	F	4	1	14·1		
Battery chemicals	M	16	39	1·5	1·3	0·7–2·4
Plastic production	M	14	25	2·0	1·7	0·9–3·4
	F	1	1	3·3		
Cleaning chemicals	M	2	12	0·6	0·3	0·1–1·4
	F	0	7			
Gas	M	30	67	1·6	1·4	0·9–2·2
	F	0	2			
Acids/lye	M	36	100	1·3	1·3	0·9–1·9
	F	7	9	2·8		
Organic solvents	M	29	108	0·9	0·9	0·6–1·5
	F	2	8	0·8		
Oil	M	37	84	1·6	1·4	0·9–2·1
	F	0	1			
Asbestos	M	17	34	1·8	1·8	1·0–3·4
Weed killers	M	18	52	1·2	1·1	0·6–2·0
	F	0	1			
Wool dust	M	11	24	1·6	1·4	0·8–2·7
	F	5	13	1·3		
Cotton dust	M	13	29	1·6	1·5	0·8–2·6
	F	7	17	1·4		
Any occupational dust	M	111	289	1·6	1·6	1·2–2·0
	F	10	23	1·5		

*Adjusted for age, tobacco, and alcohol consumption (and sex when relevant).

risk ratio of 1·8 compared with all not exposed to asbestos, which was borderline statistically significant.

By counting any exposure to potential chromium containing compounds (cement, antirust chemicals, woodstain, chromium plating baths, and textile dyes) as chromium exposure, an adjusted risk ratio of 1·1 (0·8–1·5) was estimated for the exposed compared with all others. The unadjusted risk ratio was 1·2 for men and 1·7 for women.

Exposure to nickel grouped in like manner based on the potential nickel containing compounds alloys, battery chemicals, and chemicals used in the production of plastics are an estimated adjusted risk ratio of 1·7 (1·2–2·5) for the exposed compared with all others. Men had an unadjusted risk ratio of 1·7 and women one of 8·9 (five out of seven exposed women belonged to the cancer group), both values are statistically significant at the 5% level.

The remaining tables are based on the longest held occupations. Patients with cancer more often described this work as being dirty, physically hard, and predominantly out of doors ($p<0·05$).

Table 4 presents risk ratio according to the longest held occupational unit. Only drivers (except bus drivers) had an increased risk ratio whose 95% confidence interval did not include 1·0.

In table 4 the respondent's work experience is also grouped according to the International Standard Industrial Classification (five digits) and the less comprehensive (two digits) industrial classification worked out by the Danish factory inspectorate. Workers in the manufacturing of concrete and cement including asbestos cement had a considerably increased risk ratio of laryngeal cancer. A statistically significant increased risk of laryngeal cancer is also seen for people working in the carrier van and transportation of goods business. Table 4 also shows that men working at the harbours had an increased risk of getting laryngeal cancer.

Discussion

This study supports previous findings of high risks for laryngeal cancer among drivers,[21] and especially the high risk for workers producing cement concrete and asbestos cement.[7] At least some of the workers producing concrete have been exposed to asbestos. Drivers have probably also, to some extent, been exposed to asbestos stemming from brake linings, but other risk factors should also be considered.

The "longest held " jobs were considered to be more relevant as possible sources of carcinogenic exposures than were jobs held just before diagnosis: this does not, however, rule out that important occupations and occupational exposures were overlooked.

Information on occupation is probably not biased by the disease state: most people are able to report their main occupation and only a few know anything

Table 4 *Longest held occupations (among those represented by at least seven people) with significant risk ratios*

	Sex	No of subjects: Cases	No of subjects: Controls	Risk ratios†: Unadjusted	Risk ratios†: Adjusted	95% Confidence limit for adjusted risk ratio
Occupational unit (among 46 examined)*						
Drivers (except bus drivers)	M	7	6	4·2	3·2	1·1–9·7
	F	0	1	—		
Industries classified by ISIC (among 39 examined)						
Manufacture of non-metallic mineral products	M	5	1	17·9	28·4	3·3–
	F	0	0			
Freight transport by road	M	13	11	3·1	2·3	1·0–5·3
	F	0	0			
Industries classified by Danish Work Inspectorate Classification (among 41 examined)*						
Concrete and cement manufacture	M	6	2	10·8	17·3	3·3–3·6
	F	0	0	—		
Freight transport by road	M	18	30	2·2	1·6	0·9–3·6
	F	0	1			
Port service	M	6	4	5·4	4·8	1·3–17·7
	F	0	0			
Taxi service and miscellaneous types of transport	M	10	12	3·0	2·5	1·0–6·2
	F	0	0			
Hotels and restaurants	M	4	6	2·4	2·7	1·0–7·2
	F	5	3	5·9		

*Complete tables are available on request.
†Adjusted for age and tobacco and alcohol consumption.

about the occupational risk factor for laryngeal cancer. Information on occupational exposures is more vulnerable to recall bias. The patients with cancer more frequently described the occupation as dusty, dirty, and physically demanding. This might indicate information bias, but it agrees with the finding that patients with cancer more often belong to the lower social classes.

Interestingly, this social class association apparently is not only the result of confounding with alcohol and tobacco use. High risk ratios remain after adjusting not only for amounts of alcohol and tobacco consumed but also for preferred type of alcoholic beverage.

Dust or dirt in general are unlikely to be carcinogenic but they may promote the effect of carcinogenic agents—for instance, tobacco smoke. If that was the case one would expect a relative risk of unity for the non-smokers and a raised risk for the smokers. No support for this was found from the data, however.

The unequal distribution of non-respondents among cases and controls does, without any doubt, bias the result. We believe that controls who never had been exposed to any of the chemicals mentioned in the questionnaire were less likely to respond. If this is true many of the reported risk ratios are underestimated. Some, however, will be biased towards high values (for farmers and fishermen, for example, if these occupations are overrepresented in the group of non-respondents). The high risk ratio for drivers could be the result from non-respondents' bias, but the non-respondents' bias does not explain why this risk was increased mainly for truck drivers.

The present data provide only a modest amount of information on the effect of type of employment on laryngeal cancer risk, reflecting the difficulty in studying the relation between rare exposures and rare diseases. Table 4 shows that only about 40 occupational or industrial groups were represented by at least seven people. Thus the information obtained is sparse, as indicated by wide confidence limits, and controlling for confounding is only possible to a limited extent. Several potential occupational risk factors could easily be overlooked in a study such as this, and the fraction of cancer attributable to occupation could be much larger than indicated here. Laryngeal cancer is more frequent among working class men compared with other men and much more frequent among men than women. These differences persist after controlling for smoking and drinking habits. Alternative explanations should include occupational exposures.

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References

[1] Stell PM, McGill T, Asbestos and laryngeal carcinoma. *Lancet* 1973; i: 416–7.
[2] Newhouse ML, Asbestos and laryngeal carcinoma. *Lancet* 1973; ii: 615.
[3] Guidotti TL. Asbestos exposure and cancer of the larynx. *The Western Journal of Medicine* 1975; **122:** 75.
[4] Shettigara PT, Morgan RW. Asbestos, smoking, and laryngeal carcinoma. *Arch Environ Health* 1975; **30:** 517–9.
[5] Morgan RW, Shettigara PT. Occupational asbestos exposure, smoking, and laryngeal carcinoma. *Ann NY Acad Sci* 1976; **271:** 308–10.
[6] Blot WJ, Morris LE, Stroube R, *et al.* Lung and laryngeal cancers in relation to shipyard employment in coastal Virginia. *J Natl Cancer Inst* 1980; **65:** 571–5.
[7] Clemmensen J, Hjalgrim-Jensen S. Cancer incidence among 5686 asbestos-cement workers followed from 1943 through 1976. *Ecotoxicology and Environmental Safety* 1981; **5:** 15–23.
[8] Newhouse ML, Gregory MM, Shannon H. Etiology of carcinoma of the larynx. *IARC Scientific Publications* 1980; **2:** 687–95.
[9] Wynder EL, Bross IJ, Emerson D. A study of environmental factors in cancer of the larynx. *Cancer* 1956; **9:** 86–110.
[10] Chovil A. Laryngeal cancer: an explanation for the apparent occupational association. *Medical Hypotheses* 1981; **7:** 951–6.
[11] Lynch J, Hanis NM, Bird MG, Murray KJ, Walch JP. An association of upper respiratory cancer with exposure to diethyl sulfate. *JOM* 1979; **21:** 333–41.
[12] Manning KP, Skegg DCG, Stell PM, Doll R. Cancer of the larynx and other occupational hazards of mustard gas workers. *Clin Otolaryngol* 1981; **6:** 165–7.
[13] Pedersen E. Cancer of respiratory organs among workers at a nickel refinery in Norway. *Int J Cancer* 1973; **12:** 32–41.
[14] Englund A. Cancer incidence among painters and some allied trades. *J Toxicol Environ Health* 1980; **6:** 1267–73.
[15] Flanders WD, Rothman KJ. Occupational risk for laryngeal cancer. *Am J Public Health* 1982; **72:** 369–72.
[16] Danish Cancer Registry. *Incidence of cancer in Denmark 1973–77.* Copenhagen: Danish Cancer Society, 1982.
[17] Olsen J, Sabroe S, Lajer M. Welding and cancer of the larynx. *Eur J Cancer Clin Oncol* (in press).
[18] Sidenius K, Sørensen KK, Svane O. Strubekræft blandt metalarbejdere. *Ugeskr Læg* 1983; **145:** 1623–8.
[19] *Dansk Fagkode* København: Arbejdsdirektoratet, 1979.
[20] *Erhvervsgrupperingskode* Danmarks Statistik, 1977.
[21] *Fortegnelse over virksomhedsgrupper.* København: Arbejdstilsynet, 1956.
[22] Breslow NE, Day NE. *Statistical methods in cancer research.* Lyon: International Agency for Research on Cancer, 1980.
[23] Thomas DG. Exact confidence limits for the odds ratio in a 2 × 2 table. *Applied Statistics* 1971; **20:** 105–10.