Eur J Cancer Clin Oncol, Vol. 20, No. 5, pp. 639–643, 1984.
Printed in Great Britain.

0277-5379/84$3.00+0.00

Welding and Cancer of the Larynx: a Case-control Study*

JØRN OLSEN,†‡ SVEND SABROE§ and MATHILDE LAJER§

*†*Institute of Community Health, Department of Social Medicine, University of Odense, J. B. Winsløwsvej 17, 5000 Odense, Denmark and §Institute of Social Medicine, University of Aarhus, Vesterbro Torv 1–3, 8000 Århus C, Denmark*

Abstract—*The purpose of the study was to examine the occupational history of laryngeal cancer patients, and especially their exposure to welding. The investigation was conducted as a case-control study where all newly diagnosed patients less than 75 yr of age with cancer of the larynx in Denmark during March 1980 to March 1982 were selected as cases. For each case, four age- and sex-matched controls were identified from the municipal person register in which the case was listed. Data were collected partly by means of questionnaires and partly by abstracting information from the medical records of cases. Workers exposed to welding fumes had a slightly increased risk of cancer of the larynx, most predominantly of cancer of the subglottic area.*

INTRODUCTION

THE INCIDENCE rate of cancer of the larynx has been increasing in Denmark. During the period 1973–1977 the annual incidence of cancer of the glottic was 10–20 per 100,000 men at 60–70 yr of age compared to about 5 per 100,000 women of the same age group. Cancer of the subglottic or supraglottic has an incidence of 10–30 per 100,000 men at 60–70 of yr of age whereas for women the corresponding age-specific incidence rate is approximately 2–3 per 100,000 (The Danish Cancer Registry).

These sex differences suggest that occupational factors might play a role in the etiology of cancer of the larynx along with the already well-documented role of alcohol and tobacco [1–4].

An unexpectedly large number of larynx cancer cases has been reported by the Danish occupational health agency in a workplace where a large number of employees were engaged in welding [5]. This finding prompted the present study.

The aim of this investigation was to study the occupational histories of larynx cancer patients with special interest in their exposure to welding fumes.

Accepted 11 October 1983.
*The study was supported by grants from the Danish Medical Research Council (13-9449, 13-2819)
‡To whom correspondence and requests for reprints should be addressed.

MATERIALS AND METHODS

The study was designed as a case-control study. All newly diagnosed larynx cancer patients in Denmark during the period of March 1980 to March 1982 who were under 75 yr of age at the time when being diagnosed were selected as cases. The cancer patients were ascertained from the hospital departments (five) involved in laryngeal cancer therapy in Denmark. None were members of the cluster [5] that initiated the study. For each case four control persons were identified using the municipal person-registry in which the case was listed. Controls were matched to cases according to residence, sex and closest possible birth date.

Both cases and controls received a questionnaire that included questions about their exposure to a number of specific chemical and physical agents and use of tobacco and alcohol. Information from the medical records of cases was abstracted by nurses collaborating with the project. Since only a few females had been exposed to welding fumes this study is restricted to males only. Twelve out of 316 male cases (4%) refused to participate in the study, as did 277 out of 1248 male controls (22%). In the control group the refusal rate was higher in the rural districts (24%) than in the Copenhagen area (16%) and, furthermore, it was highest among the elderly.

The site of origin of larynx cancer in cases was distributed as follows: in 176 cases the cancer

originated from the glottic, in 79 from the supraglottic, in 11 from the subglottic and in 5 the site of origin could not be classified. Twenty-six patients had cancer of the hypopharynx and 2 patients had cancer of the oropharynx. These 28 cases were excluded from the case group.

In 92% of the remaining 271 cases the cancer was of the plano-cellular type.

The controls were contacted up to three times in an effort to enlist their cooperation. Questionnaires with missing answers were returned or the person was interviewed about them by telephone. Some of the cases were also interviewed. In spite of this, information on alcohol use was not obtained from 5% of the participating cases and 9% of the controls; information on smoking was missing for 2% of the cases and 3% of the controls; and information on welding was missing for 4% of the cases and 5% of controls.

The unit of measurement of alcohol is 10 g (equivalent approximately to the content of one beer, one glass of wine or one schnapps). The unit of measurement of tobacco is 1 g, equivalent to the tobacco content of one cigarette. The tobacco content of a cigar was set at 3 g and a pipeful at 2.5 g.

For the statistical analyses the Mantel–Haenszel test [6] was used along with logistic regression [7]. 'Exact confidence limits' are given for the unadjusted relative risks [8]. In most of the analyses no account was taken of the matching on age and residence. However, analysis of matched data with a variable number of controls was performed in Table 1 [7, pp. 176–182].

RESULTS

As shown in Table 1, men exposed to welding fumes at their workplace had a borderline statistically significant risk of getting cancer of the larynx. Five out of 11 patients with a cancer that originated from the subglottis had been exposed to welding fumes, and this finding is statistically significant at the 5% level. It is seen that when cases are compared only with the matched controls statistically significant relative risks are found for all laryngeal cancer, cancer of the supraglottis and cancer of the subglottis.

Among all the exposed cancer patients 50% welded more than 15 hr weekly, compared to only 21% of the welders in the control group ($P < 0.05$). Welders in the case group had been welding for 22 yr on average, compared to 18 yr for welders in the control group. The cases had a tendency to weld painted material, as well as using basic electrodes more frequently and welding in rooms without ventilation systems, although these differences were not statistically significant at the 5% level.

In Table 2 the association between the duration of welding exposure and cancer of the larynx is shown. It is seen that the number of welding hours per week given as an average for the time the respondents have been welding is a more powerful predictor of laryngeal cancer than the number of welding years. Here, too, the weakest association between welding exposure and cancer of the larynx is seen for the subgroup of patients with cancer of the glottis.

In Table 3 it is shown that the increased risk of laryngeal cancer among welders is seen only for the smokers, but the interpretation of that finding is hampered by the fact that only 13 of the cancer patients were nonsmokers.

In Table 4 a similar analysis as given in Table 1 is shown, but concerning welding in stainless steel. As expected, only a few workers had welded in stainless steel, and the statistical analysis gives very inprecise estimates, as illustrated by the wide confidence intervals. A borderline statistically significant association between cancer of the subglottis region and welding of stainless steel is found, however.

DISCUSSION

This study supports to some extent the hypothesis that exposure to welding fumes increases the risk of laryngeal cancer. Other studies have shown an association between

Table 1. Estimated relative risks (RR) for cancer of the larynx among males exposed to welding fumes at the worksite (95% confidence limits in parentheses)

					Analysis unmatched data		Matched data
	Cancer patients		Controls		Unadjusted	Adjusted	Unadjusted
Type of cancer	Total	Exposed	Total	Exposed	RR	RR*	RR
All cancer patients	271	42	971	115	1.4(0.9–3.0)	1.3(0.9–2.0)	1.6(1.0–2.4)
Glottic	176	23	971	115	1.1(0.7–1.8)	1.1(0.7–1.8)	1.2(0.7–2.1)
Supraglottic	79	13	971	115	1.5(0.7–2.8)	1.5(0.8–2.9)	2.2(1.0–5.0)
Subglottic	11	5	971	115	6.2(1.5–24.8)	6.3(1.8–21.6)	8.1(1.5–43.3)

*Ajusted for age in years, and average alcohol and tobacco consumption (4 categories, unknown coded in low category, unknown welding exposure coded as no exposure). Logistic regression.

Table 2. Relative risk (RR) according to welding exposure (males only; logistic regression; stepwise exclusion of welding years and welding exposure)

Predictor	RR All cancer sites				Glottic			Supra-glottic			Subglottic		
Intercept	0.05	0.05	0.06	0.04	0.04	0.05	0.01	0.01	0.01	0.02	0.01	0.02	
Age in years	1.01	1.01	1.01	1.01	1.01	1.01	1.03	1.03	1.03	0.99	1.00	0.99	
Tobacco use (1)	1.69	1.69	1.71	1.74	1.74	1.74	1.61	1.61	1.65	0.93	0.95	0.99	
Alcohol consumption (2)	1.24	1.24	1.24	1.28	1.27	1.27	1.16	1.16	1.16	1.16	1.15	1.14	
Weekly welding exposure (3)	1.22	1.28		1.08	1.18		1.64	1.45		1.32	1.93		
Welding years (4)	1.03			1.05			0.91			1.27			
Δ_G (d.f. = 1)		0.26	5.23		0.31	1.48		0.79	4.77		1.85	3.09	
P value		>0.05	<0.025		>0.05	>0.08		>0.05	<0.05		>0.05	>0.05	

Coded: (1) g/day: 0 = 0, 1 = 1–9, 2 = 10–19, 3 = 20+; (2) g/day: 0 = 0–9, 1 = 10–19, 2 = 20–29, 3 = 30+; (3) hr: 0 = 0, 1 = 0–4, 2 = 5–14, 3 = 15+; (4) 5 yr groups: 0 = 0–4, 1 = 5–9 and so on.

welding exposure and lung cancer morbidity or mortality [9–13].

It was expected that welding of stainless steel, which leads to exposure to the carcinogenic hexavalent chrome and nickel, would carry the greatest risk, but this hypothesis was not supported by the study. The finding is not conclusive, though, in light of the relatively small number of people in the study material engaged in welding of stainless steel.

This study shows no strong association between cancer of the larynx and welding (except for the very rare cancer of the subglottic region). Recall bias might be responsible for the association, even though the cases were given the questionnaires as soon as possible after having been diagnosed. If recall bias exists we would expect cases to remember even short-term welding exposures better than controls. The data given in Table 1 have therefore been re-analysed, putting all exposed less than 5 yr in the non-exposure category. Using a logistic regression model adjusting for age, smoking and drinking habits, we found a relative risk for all cancer sites of 1.5 (1.0–2.3), cancer of the glottic 1.4 (0.8–2.2), cancer of the supraglottic 1.4 (0.7–2.7) and cancer of the subglottic 8.1 (2.4–27.6). Of all the men in the study, 26 had welded less than 5 yr. All the exposed subglottic patients had been exposed for more than 5 yr, but it is still difficult to know the importance of this unexpectedly high relative risk for this group. Only 11 males were diagnosed as subglottic cancer patients, and it is obvious that little adjustment for potential confounders and only imprecisely estimated confidence limits can be obtained in the regression model.

Cases and controls were asked to give information on a number of occupational exposures, not only welding fumes. Most of these exposures occurred with equal frequency among cases and controls, indicating no sign of general recall bias. In the introduction the participants were told that this was a study of the occupational etiology of cancer of the larynx, but the welding hypothesis was not mentioned.

The total number of non-respondents is within acceptable limits, but it is admittedly unequally distributed among cases and controls, which is one of the drawbacks of using population controls. A high proportion of welders among the non-respondents in the control group could explain the present finding. However, we think it is more likely that the bias has the opposite direction. It is our experience that the people selected for the study who had not been occupationally exposed to any of the potential hazards mentioned in the questionnaire were less likely to respond. This experience is in agreement

Table 3. Estimated relative risks (RR) for cancer of the larynx among males exposed to welding dust by average tobacco consumption (95% confidence limits in parantheses)

Average tobacco consumption (g/day)	Cancer patients Total	Cancer patients Exposed	Controls Total	Controls Exposed	Unadjusted RR
0	13	0	196	17	0.0(0.0–3.8)
1–9 (+ unknown)	136	20	485	61	1.2(0.7–2.1)
10+	127	22	290	37	1.4(0.8–2.6)

Table 4. Estimated relative risk (RR) for cancer of the larynx among males exposed to welding dust from stainless steel (95% confidence limits in parentheses)

Type of cancer	Cancer patients Total	Cancer patients Exposed	Controls Total	Controls Exposed	Unadjusted RR	Adjusted RR*
All cancer patients	271	12	971	30	1.5(0.7–3.0)	1.3(0.7–2.7)
Glottic	176	8	971	30	1.5(0.6–3.4)	1.3(0.6–3.1)
Supraglottic	79	2	971	30	1.2(0.3–10.8)	0.7(0.2–3.2)
Subglottic	11	2	971	30	7.0(0.7–35.7)	6.7(1.0–33.3)

*Adjusted for age in years, and average alcohol and tobacco consumption (4 categories, unknown coded in low category). Logistic regression.

with the finding that most of the non-respondents came from the agricultural areas of the country.

Non-response concerning welding exposure is coded as no exposure in the analysis. This is done because most of the people had occupations which were unlikely to involve any welding fume exposure. In fact, only four of these people worked in metal industries, and 30% of the non-response group worked as farmers or fishermen. Nevertheless, all the data have also been analysed excluding the non-response group, and similar results were found as presented in this paper.

Unknown alcohol and tobacco consumption was coded in the low categories, because most of the unknowns appeared to belong to that group. However, all the adjusted risk ratios remained substantially the same when the unknowns were excluded from the data set.

Welding results in a complex mixture of gases, oxides and other compounds such as O_3, NO_2, Cr, V, As, Mn, Ni, Be, Cu, Na, K, Si, F and Pb. The chemistry is determined by the technology, materials and welding parameters used, e.g. welding with basic electrodes gives off flourides [14] and welding of painted materials results in exposure to paint pigments (including lead, chrome and zinc), as well as a number of organic by-products of chemical reactions.

Exposure to welding fumes represents a potential source of health risk to a significant number of workers, but in spite of this little research has been done to identify and quantify the risk.

Acknowledgements—The authors wish to thank the following people for their cooperation: Anni Overdal Poulson, Kirsten Haue-Pedersen, Hanne Lundsgaard Jensen, Meta Thye Pedersen, Inge Kejlstrup, Ulla Fasting, Bente Bislev, Margrethe Larsen, Birgit Jansen, Karen Kristensen, Karen Petersen, Kirsten Pryds Jensen, Kirsten Bork Nielsen, Hanne Sand Hansen and Birthe Dam Nielsen.

REFERENCES

1. Wynder EL, Bross IJ, Day E. A study of environmental factors in cancer of the larynx. *Cancer* 1956, **9**, 86–110.
2. Wynder EL, Covey LS, Mabuchi K, Mushinski M. Environmental factors in cancer of the larynx. *Cancer* 1976, **38**, 1591–1601.
3. Hinds MW, Thomas DB, O'Reilly HP. Asbestos, dental X-rays, tobacco, and alcohol in the epidemiology of laryngeal cancer. *Cancer* 1979, **44**, 1114–1120.
4. Rothman KJ, Cann CI, Flanders D, Fried MP. Epidemiology of laryngeal cancer. *Cancer* 1980, **2**, 195–209.
5. Sidenius K, Sørensen HH, Svane O. Cancer of the larynx among metalworkers. *Ugeskr Læger* 1983, **145**, 1623–1628.

6. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *JNCI* 1959, **22,** 719–748.
7. Breslow NE, Day NE. *Statistical Methods in Cancer Research.* Lyon, IARC, 1980.
8. Thomas DG. Exact confidence limits for the odds ratio in a 2×2 table. *Appl Statist* 1970, **20,** 105–110.
9. Office of Population Censuses and Surveys. *Occupational Mortality. The Registrar General's Decennial Supplement for England and Wales, 1970/72.* London, HMSO, 1978.
10. Beaumont JJ, Weiss NS. Mortality of welders, shipfitters, and other metal trades workers in boilermaker. *Am J Epidemiolist* In press.
11. Menck HR, Henderson BE. Occupational differences in rates of lung cancer. *J Occup Med* 1976, **18,** 797–801.
12. Breslow L, Hoaglin L, Rasmussen G, Abrahms HK. Occupations and cigarette smoking as factors in lung cancer. *Am J Publ Health* 1954, **44,** 171–181.
13. Milham S Jr. Cancer mortality patterns associated with exposure to metals. *Ann NY Acad Sci* 1976, **271,** 243–249.
14. Stern RM. Process-dependent risk of delayed health effects for welders. *Environ Health Perspect* 1981, **41**, 235–253.