Laryngeal and hypopharyngeal cancer and occupation: results of a case-control study

Paquerette Goldberg, Annette Leclerc, Danièle Luce, Jean-François Morcet, Jacques Brugère

Abstract

***Objectives*—To ascertain whether certain occupations are associated with laryngeal or hypopharyngeal cancer.**

***Methods*—A hospital based case-control study was carried out in 15 hospitals in France. It included 528 male cases diagnosed between January 1989 and April 1991, and 305 male controls with various other types of cancer. Interviews were carried out to obtain lifetime job histories and information on potential confounders. Logistic regression was used to compute the odds ratios (OR) for each of about 80 occupations and industries.**

***Results*—There was an excess risk of laryngeal and hypopharyngeal cancer among service workers (OR 2.2, 95% confidence interval (95% CI) 1.3 to 3.9), agricultural and animal husbandry workers (OR 1.6, 95% CI 0.9 to 2.8), miners and quarrymen (OR 2.0, 95% CI 0.9 to 4.3), plumbers and pipe fitters (OR 2.6, 95% CI 0.8 to 8.1), glass formers and potters (OR 4.3, 95% CI 1.0 to 18), transport equipment operators (OR 1.5, 95% CI 1.0 to 2.5), and unskilled workers (OR 1.7, 95% CI 1.0 to 2.9). Analysis by industrial branch showed an excess risk for coal mining (OR 2.1, 95% CI 1.1 to 4.1), manufacture of metal products (OR 1.9, 95% CI 1.0 to 3.3), and administration and sanitary services (OR 1.7, 95% CI 1.1 to 2.5).**

***Conclusion*—These results suggest that occupational exposure might have a role in generating laryngeal and hypopharyngeal cancer, and indicate the need for further evaluation of these findings, and for the identification of the carcinogens which might account for the excess risks found for certain occupations.**

INSERM Unité 88, 14 rue du Val d'Osne, 94410 Saint-Maurice, France
P Goldberg
A Leclerc
D Luce
J-F Morcet

Institut Curie, 26 rue d'Ulm, 75005 Paris, France
J Brugère

Correspondence to:
Dr Paquerette Goldberg, INSERM Unité 88, Hopital National de Saint-Maurice, 14 rue du Val d'Osne, 94415 Saint-Maurice Cedex, France.

Accepted 26 February 1997

(*Occup Environ Med* 1997;54:477–482)

Keywords: epidemiological study; occupational risk factor; anatomical site

During the period from 1983 to 1987, the annual age standardised incidence of laryngeal cancer among men varied from four to six per 100 000 in most European countries, but was as high as 12 per 100 000 in Italy and France.[1] For the hypopharynx, the age standardised incidence in France (8.6 per 100 000 men-years) was higher than in the other European countries,[1] where it varied from 0.7 to 1.2. For the white male population of the United States, the age standardised incidences from 1983 to 1987 were 6.8 and 1.5 respectively (for 100 000 men-years) for cancer of the larynx and hypopharynx.

Tobacco smoking and alcohol consumption have been established as the main risk factors for laryngeal and hypopharyngeal cancers.[2 3] A multicentre study coordinated by the International Agency for Research on Cancer (IARC) in six populations of southern Europe[4] showed that the risk associated with a high level of alcohol consumption (more than a litre of wine a day or equivalent) rose about twofold for the larynx and about fourfold for the hypopharynx compared with the risk for smaller consumers. In the same study, the consumption of more than 25 cigarettes a day was associated with a risk of laryngeal or hypopharyngeal cancer 16 times greater than the risk for non-smokers. Comparable results have been established in other studies.[5–8]

As the studies on occupational risk factors for laryngeal cancer[9–12] or pharyngeal cancer[13 14] have produced conflicting results, the existence and magnitude of certain associations between the risk factors studied and these diseases are still questionable, as shown in a review of the epidemiological literature on the occupational factors for cancers of the upper respiratory tract.[15] The aim of the present analysis of a case-control study by job title was therefore to provide additional information about the occupational risk factors for laryngeal and pharyngeal cancer.

Subjects and methods

Cases were male patients with primary malignancies of the hypopharynx and the larynx diagnosed between 1 January 1989 and 30 April 1991; for the hypopharynx, the cases were collected over a shorter period, so that their number did not exceed half the total number of cases collected. In all, 664 patients, all resident in France, were identified for study in the 15 participating hospitals. However, 11 of them (1.6%) died before an interview could be completed, 40 (6%) could not be interviewed for health reasons, 63 (9.5%) could not be located, and 22 (3.3%) refused to participate. Finally, therefore, 528 histologically confirmed cases of squamous cell cancer were included in the study. Of these, 300 affected the larynx (196 the endolarynx, and 104 the epilarynx), 206 the hypopharynx, and 22 were cases of unspecified or synchronous cancers of the larynx and hypopharynx. The coding scheme for sites and subsites was that used by Tuyns *et al*[4]: the endolarynx includes the supraglottis (international classification of

Table 1 Laryngeal and hypopharyngeal cancer and occupation, France (1989-91) characteristics of cases and controls

	Cases		Controls	
	n	(%)	*n*	(%)
Region:				
Lille	149	(28.2)	76	(24.9)
Strasbourg	99	(18.8)	58	(19.0)
Paris	96	(18.2)	68	(22.3)
Bordeaux	80	(15.2)	46	(15.1)
Nantes	68	(12.8)	33	(10.8)
Caen	36	(6.8)	24	(7.9)
Age at diagnosis (y):				
<50	107	(20.3)	42	(13.8)
50-59	190	(36.0)	88	(28.9)
60-69	172	(32.6)	101	(33.1)
≥70	59	(11.2)	74	(24.3)
Mean	58.0		60.7	
Level of education:				
Primary	317	(60.0)	137	(44.9)
Lower vocational	144	(27.3)	84	(27.5)
Lower secondary	19	(3.6)	23	(7.5)
Upper secondary	16	(3.0)	15	(4.9)
Upper vocational	17	(3.2)	12	(3.9)
University	15	(2.8)	33	(10.8)
Other	—		1	(0.3)
Tobacco smoking (pack-years):				
Data missing	—	(0.6)	1	(0.3)
Non-smoker	15	(2.8)	82	(26.9)
1-29	130	(24.4)	112	(36.7)
30-45	138	(26.1)	61	(20.0)
≥45	245	(46.0)	49	(16.1)
Alcohol consumption (glasses/day):				
Data missing, abstainers	24	(4.5)	9	(3.0)
Occasional and 1-2	77	(14.8)	112	(36.7)
3-4	80	(15.2)	61	(20.0)
5-8	158	(29.8)	74	(24.3)
9-12	109	(20.6)	31	(10.2)
≥12	80	(15.2)	18	(5.9)
Total	528		305	

diseases ninth revision (ICD-9) 161.1), glottis (ICD-9 161.0), subglottis (ICD-9 161.2), and endolarynx unspecified (ICD-9 161.8–9), the epilarynx includes the free border of the epiglottis (ICD-9 146.4), the posterior surface of the suprahyoid portion (ICD-9 161.1), the junctional region of three folds (ICD-9 146.5), the aryepiglottic fold, the arytenoid and interarytenoid incisure (ICD-9 161.1, 148.2), and the epilarynx unspecified (ICD-9 149.8, 195.0), and the hypopharynx includes the piriform sinus (ICD-9 148.1), the post-cricoid area (ICD-9 148.0), the posterior wall (ICD-9 148.3), and the hypopharynx unspecified (ICD-9 149.8).

This study on laryngeal and hypopharyngeal cancer was part of a larger one on the occupational risks of cancer of the upper respiratory tract (sinonasal cavities, larynx, and hypopharynx). For practical reasons, controls were selected during the 1987–91 period, and consisted of patients in hospital selected to be comparable with the cases. Thus, controls were male patients with primary cancer selected by frequency matching for age, with a control to case ratio of about 1:1 for the larynx, and 3:2 for the hypopharynx. To obtain comparable catchment areas for cases and controls, the controls were patients with types of cancer requiring the same medical environment as the cases. The hospital departments concerned were specialised departments in the public or semipublic sector, located in the same hospitals as the cases, or in similar hospitals nearby. All the eligible controls were identified on the admission lists of these departments as patients without previous treatment for the pathology that caused the admission to hospital, with characteristics corresponding to the inclusion criteria. Identification through hospital admission lists had already been used by others,[7 10] and led here to the recruitment of 355 eligible controls. However, 50 of them (14%) could not be interviewed (14 for health reasons, 22 could not be located, and 14 refused), so that 305 were actually included in the study.

Controls were patients with primary cancer of 15 sites: rectum or anal canal (n=30), liver or gall bladder (n=15), pancreas (n=11), haematopoietic system (n=34), bones or cartilage (n=7), soft tissues (n=11), melanoma (n=18), prostate (n=63), testis (n=17), bladder (n=29), other urinary organs (n=27), brain or nervous system (n=18), thyroid (n=18), colon (n=5), and stomach (n=2).

Table 1 shows the regional distribution of controls and cases. As the distribution was similar according to the region, adjustment for this variable was considered unnecessary.

Personal interviews were conducted with each subject. The questionnaire covered demographic characteristics, detailed alcohol consumption, and tobacco smoking, and detailed lifetime occupational history, including job titles and description of tasks performed. For this history, a questionnaire close to that elaborated in Montreal by Gérin and Siemiatycki,[16] was used, to collect detailed information on all jobs held for six months or longer. This questionnaire had already been used in French studies.[17]

Jobs were coded according to the 1968 international standard classification of occupations (ISCO) of the international labour organisation (ILO code 1968)[18] and the industrial branches, according to the United Nations international standard industrial classification (ISIC) code.[19] To obtain sufficient numbers for analyses, jobs were grouped into 51 categories and industries into 44, largely on the basis of the subheadings.

Analyses were conducted for the larynx and hypopharynx together, with the same control group, because of the contiguity of these anatomical sites and the similarity of their main risk factors (alcohol and tobacco). Also, odds ratios (ORs) were computed for each of the three subsites (endolarynx, epilarynx, and hypopharynx).

Two kinds of occupational variable were used for the analyses: having ever (*v* never) worked in a selected occupation, and having ever (*v* never) worked in a selected industry. For each occupation, the period of first employment, in two categories (until 1945, and as from 1946), was also analysed to find possible differences between the risks of these periods. Similarly, analyses were performed according to the duration of employment, into two classes (<9 years, and ≥10 years), to find possible dose-response effects. To allow for any induction and latency effects, analyses were also performed after excluding all exposure during the 10 years immediately preceding diagnosis.

Table 2 Laryngeal and hypopharyngeal cancer and occupation, France (1989–91): odds ratios by job title

Job title	ILO code 68	Cases n	Controls n	§ OR	(95% CI)	¶ OR	(95% CI)
Professionals, technicians, managers	0xx to 2xx	55	69	0.5*	(0.3 to 0.7)	0.5*	(0.3 to 0.8)
Administrative workers	3xx	90	80	0.7†	(0.4 to 1.0)	0.7†	(0.5 to 1.1)
Sales workers	4xx	54	39	0.8	(0.5 to 1.4)	0.9	(0.5 to 1.5)
Service workers	5xx	90	26	2.2*	(1.3 to 3.9)	2.2*	(1.3 to 3.9)
Farmers	60x to 61x	55	49	0.7	(0.4 to 1.1)	0.6*	(0.3 to 1.0)
Agricultural, animal husbandry workers	62x	68	27	1.6†	(0.9 to 2.8)	1.4	(0.8 to 2.4)
Forestry workers, fishermen, hunters	63x to 64x	17	8	0.9	(0.3 to 2.3)	0.8	(0.3 to 2.0)
Production supervisors	70x	13	12	0.7	(0.3 to 1.8)	0.8	(0.3 to 2.1)
Miners, quarrymen	71x	37	13	2.0†	(0.9 to 4.3)	1.8	(0.9 to 3.9)
Metal processers	72x	23	13	0.9	(0.4 to 1.9)	0.8	(0.4 to 1.7)
Wood preparation, paper workers	73x	9	8	0.4	(0.1 to 1.3)	0.4	(0.1 to 1.2)
Chemical processers	74x	10	4	1.3	(0.4 to 5.1)	1.5	(0.4 to 5.8)
Textile workers	75x	23	7	1.9	(0.7 to 5.0)	1.6	(0.6 to 4.5)
Food, drink processing (not butchers, bakers)	77x	17	6	1.8	(0.6 to 5.7)	1.9	(0.6 to 6.0)
Butchers	773	20	11	0.9	(0.4 to 2.3)	0.9	(0.4 to 2.2)
Bakers	776	22	11	1.3	(0.5 to 3.0)	1.2	(0.5 to 3.1)
Tailors, dressmakers	79x	6	4	1.3	(0.2 to 7.4)	1.2	(0.2 to 7.1)
Shoes, leather goods makers	80x	7	7	0.6	(0.2 to 2.4)	0.6	(0.2 to 2.3)
Cabinet makers	81x	17	7	1.0	(0.4 to 2.6)	1.1	(0.4 to 2.8)
Stone cutters, carvers	82x	4	1	2.9	(0.3 to 31)	2.5	(0.2 to 26)
Blacksmiths	831	18	2	3.5	(0.8 to 16)	3.1	(0.7 to 14)
Toolmakers, metal pattern makers, metal markers	832	9	4	1.2	(0.3 to 4.5)	1.5	(0.4 to 5.5)
Machine tool setter-operators	833	9	6	1.2	(0.4 to 3.9)	1.2	(0.4 to 4.1)
Machine tool operators	834	18	8	0.7	(0.3 to 1.7)	0.8	(0.3 to 1.9)
Metal grinders, polishers, tool sharpeners	835	6	2	1.7	(0.2 to 12)	1.4	(0.2 to 9.6)
Other blacksmiths, toolmakers, machine tool operator.	839	16	10	1.0	(0.4 to 2.5)	0.9	(0.4 to 2.4)
Machine fitters, machine assemblers	841	31	18	1.0	(0.5 to 2.1)	1.0	(0.5 to 2.2)
Watch clock precision instrument makers	842	3	3	0.7	(0.1 to 3.9)	0.7	(0.1 to 3.7)
Motor vehicle mechanics	843	27	16	1.1	(0.5 to 2.4)	1.2	(0.5 to 2.5)
Machine fitters, assemblers (not electric)	849	26	18	0.7	(0.3 to 1.4)	0.7	(0.3 to 1.5)
Electricians, electronicians	85x	27	16	1.1	(0.5 to 2.5)	1.2	(0.6 to 2.7)
Plumbers, pipe fitters	871	22	5	2.5	(0.8 to 7.6)	2.6†	(0.8 to 8.1)
Welders, flame cutters	872	24	8	1.8	(0.7 to 4.6)	1.9	(0.7 to 5.0)
Sheet metal workers	873	18	10	1.1	(0.4 to 3.0)	1.2	(0.4 to 3.1)
Structural metal preparers, erectors	874	6	—	‡	(0.7)	‡	(0.7)
Glass formers, potters	89x	13	4	4.3*	(1.0 to 18)	3.7†	(0.9 to 15)
Rubber plastics product makers	90x	5	4	0.6	(0.1 to 3.5)	0.6	(0.1 to 3.4)
Printers	92x	6	8	0.3†	(0.1 to 1.1)	0.3†	(0.1 to 1.2)
Painters	93x	24	11	1.2	(0.5 to 2.8)	1.1	(0.5 to 2.7)
Other production and related workers	94x	9	3	0.9	(0.2 to 3.7)	0.9	(0.2 to 3.7)
Bricklayers, stonemasons	951	55	16	1.6	(0.8 to 3.1)	1.4	(0.7 to 2.7)
Reinforced concreters, cement finishers	952	14	2	2.5	(0.5 to 11)	2.5	(0.5 to 12)
Roofers	953	5	5	0.4	(0.1 to 1.9)	0.4	(0.1 to 1.7)
Carpenters, joiners, parquetry workers	954	36	11	1.5	(0.7 to 3.3)	1.5	(0.7 to 3.2)
Plasterers	955	7	—	‡	(0.8)	‡	(0.8)
Other construction workers	956 to 959	23	8	1.2	(0.5 to 2.9)	1.2	(0.4 to 2.7)
Stationary engine operators	96x	7	1	3.4	(0.4 to 30)	3.8	(0.4 to 35)
Dockers, freight handlers	971	25	25	0.3*	(0.1 to 0.6)	0.3*	(0.1 to 0.5)
Other material handling and dockers	972 to 979	17	8	0.7	(0.3 to 1.8)	0.6	(0.2 to 1.7)
Transport equipment operators	98x	118	37	1.5†	(1.0 to 2.5)	1.4	(0.9 to 2.3)
Unskilled workers	99x	104	28	1.7*	(1.0 to 2.9)	1.6†	(0.9 to 2.6)

* $P<0.05$; † $0.05<P<0.10$; ‡ controls n = 0; § ajusted for age, drinking, smoking; ¶ and education.

Analyses were conducted with multivariate logistic regressions, and variables were calculated with EGRET software[20] with adjustments for age, drinking, smoking, and with and without adjustment for level of education. To avoid too small numbers, the analyses according to the period of first employment and the duration of employment were conducted with adjustment for age only. Age was categorised as a four class variable (<50 years, 50–59, 60–69, and ≥70 years), smoking, as a four class variable (non-smoker, <30, 30 to <45, and ≥45 pack-years), drinking, as a five class variable, in number of glasses of alcoholic beverage consumed daily (occasional drinker or one to two glasses, 3–4, 5–8, 9–12, and ≥13 glasses), and level of education, as a two class variable (primary level or less, more than primary level). Non-respondents for alcohol (n=5) and total abstainers (n=28) were excluded from the analysis. Indeed, the category of non-drinkers comprised former heavy drinkers who eventually stopped drinking alcoholic beverages due to their health. As in other studies,[10 12] ORs were not calculated when the number of exposed subjects (cases plus controls) was less than five.

Results

The main characteristics of the sample (table 1) indicate that the cases were slightly younger and less educated than the controls: thus, 60% of the cases had only primary education but 44.9% of the controls. More cases than controls were smokers and drinkers, with higher levels of consumption.

Table 2 shows, according to job title, the number of cases and controls, and the ORs and 95% confidence intervals (95% CIs), calculated with and without adjustment for education, for all sites combined. High ORs, significance at $P<0.05$, or borderline significance at $0.05<P<0.10$, were found for service workers, agricultural and animal husbandry workers, miners and quarrymen, plumbers and pipe fit-

Table 3 Laryngeal and hypopharyngeal cancer and occupation, France (1989-91): odds ratios by industrial branch

Industrial branch	ISIC code	Cases n	Controls n	(§) OR	(95% CI)	(¶) OR	(95% CI)
Agriculture	11x to 13x	132	72	1.2	(0.8 to 1.7)	1.0	(0.6 to 1.5)
Coal mining	21x	47	16	2.1*	(1.1 to 4.1)	2.0*	(1.0 to 3.8)
Other mining	22x to 29x	7	10	0.4	(0.1 to 1.4)	0.4	(0.1 to 1.3)
Manufacture of food (not bakery, alcohol)	31x	42	15	1.5	(0.8 to 3.0)	1.5	(0.7 to 3.0)
Manufacture of bakery products	3117	26	12	1.4	(0.6 to 3.2)	1.5	(0.6 to 3.4)
Alcohol industries	3131 to 3133	14	10	1.1	(0.4 to 3.1)	1.0	(0.3 to 3.1)
Spinning, weaving, finishing textiles	3211	31	15	1.2	(0.5 to 2.4)	1.0	(0.5 to 2.2)
Manufacture of textile (not spinning, weaving)	32x	8	12	0.4	(0.1 to 1.2)	0.4	(0.1 to 1.2)
Manufacture of leather footwear and repair	323 324 9511	8	11	0.9	(0.3 to 2.8)	0.9	(0.3 to 2.7)
Sawmills, wood mills	3311	30	17	0.8	(0.4 to 1.6)	0.7	(0.4 to 1.5)
Manufacture of wood (not sawmills)	33x	22	7	1.7	(0.7 to 4.5)	1.7	(0.6 to 4.4)
Manufacture of paper	341	11	2	2.4	(0.5 to 12)	2.4	(0.5 to 12)
Printing, publishing	342	13	8	0.6	(0.2 to 1.7)	0.6	(0.2 to 1.7)
Manufacture of chemical product (not fertilisers)	351 352	19	6	2.3	(0.8 to 7.1)	2.5	(0.8 to 7.7)
Manufacture of fertilisers, pesticides	3512	3	3	0.5	(0.1 to 2.8)	0.5	(0.1 to 2.8)
Manufacture of petroleum, coal products	353 354	4	3	0.4	(0.1 to 2.1)	0.4	(0.1 to 2.2)
Manufacture of rubber, plastic products	355 356	10	7	0.8	(0.2 to 2.5)	0.8	(0.2 to 2.6)
Manufacture of pottery, earthenware, glass, minerals	36x	25	13	1.3	(0.6 to 2.9)	1.1	(0.5 to 2.6)
Basic metal industries	37x	39	16	1.5	(0.7 to 2.9)	1.4	(0.7 to 2.8)
Manufacture of metal products	381	64	23	1.9*	(1.0 to 3.3)	1.9*	(1.1 to 3.4)
Manufacture of machinery (not electrical)	382	54	22	1.3	(0.7 to 2.3)	1.4	(0.7 to 2.5)
Manufacture of electrical machinery	383	13	8	0.8	(0.3 to 2.2)	0.8	(0.3 to 2.4)
Ship building	3841	11	5	0.9	(0.3 to 2.8)	0.9	(0.3 to 3.0)
Manufacture of transport equipment (not shipbuilding)	384	40	30	0.8	(0.4 to 1.5)	0.8	(0.5 to 1.5)
Other manufacturing industries	385 to 390	13	5	1.7	(0.5 to 5.7)	1.9	(0.5 to 6.5)
Electricity, gas, water	4xx	7	6	1.0	(0.3 to 3.3)	1.0	(0.3 to 3.5)
Construction	5xx	161	67	1.3	(0.9 to 1.9)	1.2	(0.8 to 1.8)
Trade	61x 62x	64	44	0.6†	(0.4 to 1.1)	0.6†	(0.4 to 1.1)
Restaurants, hotels	63x	34	8	1.9	(0.8 to 4.9)	2.0	(0.8 to 5.0)
Railway transportation	7111	30	12	1.3	(0.6 to 3.0)	1.4	(0.6 to 3.1)
Road transportation	7112 to 7114	31	11	1.0	(0.5 to 2.2)	1.0	(0.4 to 2.1)
Other transportation	7116 to 7191	16	8	0.8	(0.3 to 2.3)	0.8	(0.3 to 2.2)
Communications	72x	4	7	0.2*	(0.1 to 0.9)	0.2†	(0.1 to 1.0)
Financing, real estate services	8xx	42	31	0.6	(0.3 to 1.1)	0.7	(0.4 to 1.3)
Administration, sanitary services	91x 92x 96x	169	73	1.7*	(1.1 to 2.5)	1.7*	(1.2 to 2.5)
Education, scientific institutes	931 932	21	29	0.4*	(0.2 to 0.8)	0.5*	(0.2 to 1.0)
Medical services	933	13	13	0.6	(0.2 to 1.5)	0.7	(0.3 to 1.7)
Social services	934 to 939	5	6	0.7	(0.2 to 2.7)	0.6	(0.1 to 2.5)
Recreational services	94x	7	5	0.4	(0.1 to 1.8)	0.4	(0.1 to 1.8)
Repair (not leather, vehicles)	9512 9514 9519	7	4	1.1	(0.2 to 4.5)	1.0	(0.2 to 4.3)
Repair of motor vehicles	9513	21	16	0.9	(0.4 to 2.0)	0.9	(0.4 to 2.0)
Laundry, cleaning	952	8	—	‡	(1.0)	‡	(1.0)
Domestic services	953	6	2	2.1	(0.3 to 14)	1.8	(0.3 to 12)
Barber, beauty shops	9591	5	3	3.3	(0.6 to 18)	3.4	(0.6 to 20)

* $P<0.05$; † $0.05<P<0.10$; ‡ controls n = 0; § ajusted for age, drinking, smoking; ¶ and education.

ters, glass formers, and potters (based on 13 cases and four controls), transport equipment operators, and unskilled workers. The calculations with or without adjustment for educational led to similar results. For other occupational groups, mainly professional, technical, and administrative workers, printers, and dockers and freight handlers, ORs were significantly lower than unity or borderline.

In the analyses by anatomical subsite (results not shown), an excess risk of cancer was also found among blacksmiths for the endolarynx (OR 4.6, based on nine cases and two controls); among toolmakers, metal pattern makers, and metal markers (OR 4.1, based on four cases and four controls) for the epilarynx; and (except for butchers and bakers) among food and beverage processers (OR 4.0) and bricklayers and stonemasons (OR 3.1), for the hypopharynx.

The results according to the period of first employment (not shown) showed a significant high risk for the more recent period (1946–80), among service workers, agricultural and animal husbandry workers, miners and quarrymen, plumbers and pipe fitters, painters, and bricklayers and stonemasons. There was an excess risk for both periods among transport equipment operators and unskilled workers. The ORs were only slightly modified when allowance was made for a 10 year latency period.

When the data were analysed by duration of employment (results not shown), significantly high or borderline ORs were found for service workers, transport equipment operators, and for unskilled workers irrespective of the duration. For miners and quarrymen, there was an excess only in those employed for 10 years or more.

Table 3 shows the associations resulting from data analysis according to industrial branch, calculated with and without adjustment for education: significant or borderline excess risks were found for coal mining, manufacture of metal products, and public administration and sanitary services. For the activities of trade, communication, and education, ORs were lower than unity.

Discussion

An essential point in a case-control study is that the people selected as controls should have similar past potential exposure as the cases. In

a study based on patients in hospital, a bias could arise if the reasons for being in hospital in the public or semipublic sector departments selected for recruitment were not similar for cases and controls. In France, most cases of cancer of the larynx or hypopharynx are treated in such departments. The choice of the hospital in a given area mainly depends on medical criteria. For this reason, the list of cancer sites for the present controls was established in such a way as to ensure that cases and controls had comparable medical environments needed for treatment. Hence the choice of participating hospital services was unlikely to have been a source of bias.

The fact that the controls were recruited over a longer period than the cases might have led to a bias. However, when the controls selected during the periods 1987–8 and 1989–91 were compared, their main characteristics were found to be similar.

Another problem in such a study is the question of multiple comparisons, which may generate significant associations which occur by chance, independently of any association between exposure and disease. For this reason, each result requires careful examination and evaluation of its relevance[21] in the light of the results of previous studies and of the knowledge available about both dose-response patterns and induction time.

Comparisons with the results of previous investigations by others were complicated, because different authors used different ways of classifying the occupations, industrial branches, and anatomical sites considered here. The results previously reported for the occupational risks of laryngeal and pharyngeal cancer mostly concerned the endolarynx, which was sometimes subdivided into the glottis and supraglottis.[11 22 23] However, the investigations on the pharynx did not distinguish between the hypopharynx and oro- pharynx.[13 14 24] Also, the discrepancies between the results reported might have occurred because of statistical imprecision due to sparse data.

Previous authors found a moderate excess risk for the agricultural job categories[7 10 12 13] and it is therefore of interest to note that we found an increased risk among agricultural and animal husbandry workers, but not among farm managers and farmers. This difference might be due to higher levels and longer durations of exposure to a set of occupational or social risk factors for agricultural and animal husbandry workers.

The occupations involved in metal processing and manufacture have already been considered in different studies, including those of metal processor,[9] metal grinder,[10] and metal working machine operator.[12] In the present study, the OR for the basic metal industry was moderate (table 3), whereas the excess risk for metal product manufacturing was 1.9. Workers in these industrial branches with an excess risk were blacksmiths (OR 4.6 for the endolarynx), and toolmakers, metal pattern makers, and metal markers (OR 4.1 for the epilarynx), with higher ORs for 10 years or more of employment. In these branches, potential exposure to several substances, including metals in general, specific metals, metal dust, cutting oils, and sulphuric acid, had already been studied.[9 10 12 22 23 27 28] No strong evidence of their association with laryngeal cancer was shown, but as the results of several studies were concordant for these branches, it would be of interest to continue analysing the specific types of exposure they involve.

Plumbers and pipe fitters, previously found to be at risk of laryngeal cancer[9 12] with an excess risk when education was controlled for, as well as welders and flame cutters with a moderate OR of 1.8, might have been exposed to some of the same substances as workers in metal industries as well as specific exposure to metal fumes.

Although the role of asbestos in laryngeal cancer is still controversial[25 26] the excess risk found here for bricklayers and stonemasons (OR 3.1 for the hypopharynx) might be due to exposure to asbestos. Asbestos might also be a potential risk factor for plumbers and other workers in the construction industry, in which asbestos was much used. In several studies, the occupations relating to this industry showed associations with laryngeal cancer[5 10–12] and pharyngeal cancer.[14 24]

Contrary to previous studies, we found no risk for motor vehicle mechanics[11 12] working in automobile construction or the repair industry, in which the role of machining fluids (cutting, soluble, and synthetic oils) had been investigated.[27 28]

The present result for miners and quarrymen is consistent with the results reported elsewhere for mining occupations,[24] and so is the result for glass formers and potters.[29] Both categories were exposed to silica, which has already been considered a possible risk factor for laryngeal cancer.[24]

In agreement with other studies[7 11] in which an excess risk was found for diesel oil and gasoline fumes, we found an excess risk for transport equipment operators.

On the basis of the present results, it would be worth attempting to explain the excess risks we found, by extending the analysis to include the potential workplace carcinogens, which are still under investigation for their role in laryngeal and pharyngeal cancer.

This study was made possible by the support of the following hospital departments: Service ORL (Ear, Nose, Throat), CHR, Lille (Pr Piquet, Dr Chevalier); Service ORL, Centre Oscar Lambret, Lille (Dr Lefebvre); Service ORL, CHR Hôpital B, Lille (Pr Desaulty); Service ORL, Hôpital des Enfants, Bordeaux (Pr Traissac); Centre Hospitalier Pellegrin-Tripode, Bordeaux (Dr Stoll); Service ORL, Fondation Bergonié, Bordeaux (Dr Renaud-Salis, Dr Faucher); Hôpital Haut-Lévêque, Pessac (Pr Amouretti, Pr Couzigou); Service ORL, CHR, Strasbourg (Pr Conraux); Service de Radiothérapie, Centre Paul Strauss, Strasbourg (Dr Jung); Service ORL, Hôpital de Hautepierre, Strasbourg (Pr Klotz); Service ORL, Institut Curie, Paris (Dr Brugère); Service ORL, Hôtel Dieu, Nantes (Pr Beauvillain); Service de Radiothérapie, Centre René Gaudducheau, St Herblain, Nantes (Dr Peuvrel); Service ORL, Centre François Baclesse, Caen (Dr Blanchet); Service de Radiothérapie, Centre François Baclesse, Caen (Dr Couet). Interviews were conducted by B Agullo, J Allio, S Boulanger, JJ Chalé, N Contour, G Mamane, S Pueyo, B Weber, P Zagury. Association pour la Recherche contre le Cancer (ARC), Comité Départemental du Val d'Oise de la Ligue Nationale contre le Cancer, Ministère de la Recherche et de la Technologie.

1 Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, Powell J. *Cancer incidence in five continents.* Vol VI. Lyon: IARC, 1992.
2 International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans: alcohol drinking.* Vol 44. Lyon: IARC, 1988.
3 International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks of chemicals to humans: tobacco smoking.* Vol 38. Lyon: IARC, 1986.
4 Tuyns AJ, Esteve J, Raymond L, Berrino F, Benhamou E, Blanchet F, *et al.* Cancer of the larynx/hypopharynx, tobacco and alcohol: IARC international case-control study in Turin and Varese (Italy), Zaragoza and Navarra (Spain), Geneva (Switzerland), and Calvados (France). *Int J Cancer* 1988;**41**:483–91.
5 Guénel P, Chastang JF, Luce D, Leclerc A, Brugère J. A study of the interaction of alcohol drinking and tobacco smoking among French cases of laryngeal cancer. *J Epidemiol Community Health* 1988;**42**:350–4.
6 Blot WJ. Alcohol and cancer. *Cancer Res* 1992;**52**:S2119–23.
7 Ahrens W, Jöckel KH, Patzak W, Elsner G. Alcohol, smoking, and occupational factors in cancer of the larynx: a case-control study. *Am J Ind Med* 1991;**20**:477–93.
8 Zheng W, Blot WJ, Shu XO, Gao YT, Ji BT, Ziegler RG, Fraumeni JF. Diet and other risk factors for laryngeal cancer in Shanghai, China. *Am J Epidemiol* 1992;**136**:178–91.
9 Burch JD, Howe GR, Miller AB, Semenciw R. Tobacco, alcohol, asbestos, and nickel in the etiology of cancer of the larynx: a case-control study. *J Natl Cancer Inst* 1981;**67**: 1219–24.
10 Zagraniski RT, Kelsey JL, Walter SD. Occupational risk factors for laryngeal carcinoma: Connecticut, 1975–80. *Am J Epidemiol* 1986;**124**:67–76.
11 Muscat JE, Wynder EL. Tobacco, alcohol, asbestos, and occupational risk factors for laryngeal cancer. *Cancer* 1992; **69**:2244–51.
12 Wortley P, Vaughan TL, Davis S, Morgan MS, Thomas DB. A case-control study of occupational risk factors for laryngeal cancer. *Br J Ind Med* 1992;**49**:837–44.
13 Huebner WW, Schoenberg JB, Kelsey JL, Wilcox HB, McLaughlin JK, Greenberg RS, *et al.* Oral and pharyngeal cancer and occupation: a case-control study. *Epidemiology* 1992;**3**:300–9.
14 Maier H, Fisher G, Sennewald E, Heller WD. Berufliche Risikofaktoren für Rachenkrebs. *HNO* 1994;**42**:530–40.
15 Berrino F. Occupational factors of upper respiratory tract cancers. In: Hirsch A, Goldberg M, Martin JP, Masse R, eds. *Prevention of respiratory diseases. Lung biology in health and disease 68.* New York: M Dekker, 1993:81–96.
16 Gérin M, Siemiatycki J. The occupational questionnaire in retrospective epidemiologic studies: recent approaches in community-based studies. *Appl Occup Environ Hyg* 1991;**6**: 495–501.
17 Luce D, Leclerc A, Morcet JF, Casal-Lareo A, Gérin M, Brugère J, *et al.* Occupational risk factors for sinonasal cancer: a case-control study in France. *Am J Ind Med* 1992;**21**:163–75.
18 International Labour Office. *International standard classification of occupations.* Revised 1968. Geneva: BIT, 1969.
19 Statistical Office of the United Nations. *International standard industrial classification of all economic activities.*New-York: United Nations, 1968. (Statistical papers series M, number 4, revision 2.)
20 EGRET. *Reference manual.* Seattle: Statistics and Epidemiology Research Corporation 1985, 1989.
21 Savitz DA, Olshan AF. Multiple comparisons and related issues in the interpretation of epidemiologic data. *Am J Epidemiol* 1995;**142**:904–8.
22 Soskolne CL, Jhangri GS, Siemiatycki J, Lakhani R, Dewar R, Burch JD, *et al.* Occupational exposure to sulfuric acid in Southern Ontario, Canada, in association with laryngeal cancer. *Scand J Work Environ Health* 1992;**18**:225–32.
23 Maier H, Gewelke U, Dietz A, Thamm H, Heller WD, Weidauer H. Kehlkopfkarzinom und Berufstätigkeit Ergebnisse der Heidelberger Kehlkopfkrebsstudie. *HNO* 1992; **40**:44–51.
24 Haguenoer JM, Cordier S, Morel C, Lefebvre JL, Hémon D. Occupational risk factors for upper respiratory tract and upper digestive tract cancers. *Br J Ind Med* 1990;**47**:380–3.
25 Smith AH, Handley MA, Wood R. Epidemiological evidence indicates asbestos causes laryngeal cancer. *J Occup Med* 1990;**32**:499–507.
26 Piolatto G, Negri E, La Vecchia C, Pira E, Decarli A, Peto J. An update of cancer mortality among chrysotile asbestos miners in Balangero, nothern Italy. *Br J Ind Med* 1990;**47**: 810–4.
27 Eisen EA, Tolbert PE, Monson RR, Smith TJ. Mortality studies of machining fluid exposure in the automobile industry I: a standardized mortality ratio analysis. *Am J Ind Med* 1992;**22**:809–24.
28 Eisen EA, Tolbert PE, Hallock MF, Monson RR, Smith TJ, Woskie SR. Mortality studies of machining fluid exposure in the automobile industry III: a case-control study of larynx cancer. *Am J Ind Med* 1994;**26**:185–202.
29 Guénel P, Engholm G, Lynge E. Laryngeal cancer in Denmark: a nationwide longitudinal study based on register linkage data. *Br J Ind Med* 1990;**47**:473–9.