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Occupation and Bladder Cancer in Spain: A Multi-Centre Case-Control Study

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A case-control study on bladder cancer was carried out in four regions of Spain. The study included 497 cases (438 males and 59 females), 583 hospital controls and 530 population controls matched by sex, age and residence. The present paper reports the results of the analyses on occupational history. Among men, an increased risk of bladder cancer was found for textile workers (OR = 1.97, 95% CL 1.2–3.3), mechanics and maintenance workers (OR = 1.86, 95% CL 1.2–2.8), workers in the printing industry (OR = 2.06, 95% CL 1.0–4.3) and for managers (OR = 2.03, 95% CL 1.2–3.5). The risk was highest among those first employed in the textile industry before the age of 25 and prior to 1960. Among mechanics the risk was highest for those who started after the age of 25 and later than 1960. The OR for smokers who had also been employed in one of the high risk occupations was 7.82 (95% CL 4.4–14.0) which is compatible with a multiplicative effect of joint exposure to tobacco and occupational hazards.

There is strong scientific evidence that some aromatic amines are bladder carcinogens in humans.[1] Exposure to aromatic amines has been reported mainly from occupational settings. Epidemiological studies have estimated that 1 to 19% of bladder cancer cases can be attributed to occupational exposures depending on the proportion of the population employed in factories where aromatic amine derivatives are produced or used.[2]

Between 1955 and 1975 bladder cancer mortality in Spain increased by 60%.[3] In a previous study conducted in a small area of Catalonia[4,5] an increased risk of bladder cancer was found among subjects who had been employed in the textile industry. The present paper describes a larger multi-centre epidemiological study on bladder cancer and focuses on the analyses concerning past occupation. The study also collected information on other exposures such as active and passive smoking, diet, use of analgesics and artificial sweeteners, history of urinary infection and lithiasis.

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MATERIAL AND METHODS

The study was carried out in 1985 and 1986 in the provinces of Barcelona, Madrid, Cadiz, Guipúzcoa and Vizcaya. Ease of recruitment was based on the registers of 12 hospitals, which represented a small fraction of total hospital beds in the provinces of Madrid and Barcelona, but accounted for the great majority of hospital facilities in the provinces of Cadiz, Guipúzcoa and Vizcaya. Of the 691 cases diagnosed and identified in the hospital tumour registers, 497 cases of bladder cancer were interviewed (438 males and 59 females). For all cases, pathological confirmation had been obtained. Cases were resident in the province where the hospital was located and alive at the time of the interview. Only cases below the age of 79 were included, the mean age being 64.1. Among those interviewed, 254 (51%) were incident whilst 243 (49%) were prevalent cases (142 diagnosed in 1984 and 101 in 1983). Of the 194 cases that could not be interviewed, 103 had died, 39 could not be traced, 32 refused to answer and 20 could not be included for other reasons.

Two controls were included for each case, matched by sex and age (± 5 years). One control was selected from the admissions register of the same hospital as the case. This hospital control was selected from patients whose diagnoses excluded risk factors which may be related to those under study, eg chronic respiratory diseases, coronary heart disease, infections of the urinary tract, haematuria, and cancer of the respiratory tract. Of the 827 hospital controls selected, 583 were interviewed. Out of 244 who were not interviewed, 116 could not be located, 66 had died, 43 refused to answer and 19 were lost for other reasons. The second control was selected at random from the same section of the census or municipal register as that of the case. Of the 807 population controls selected, 530 were interviewed. Of those not interviewed, 140 could not be located, 60 refused to answer, 55 had died, and 20 were lost for other reasons. The hospital controls included 62 women and the population controls 65.

All the interviews were carried out in the subject's home by a trained interviewer. The questionnaire included a section covering occupational history for any job lasting more than six months. For each job, a note was taken of the year the job began and finished, the subject's occupation, a brief description of the work area and the specific work done, the name and address of the company and the main products manufactured or services provided.

The occupational history was coded by a person who was not aware either of the objectives of the investigation or whether the questionnaire belonged to a case or control. Coding was based on the National Classification of Occupations,[6] the Spanish equivalent of the International Classification of Occupations.[7] Industrial activities were coded according to the National Classification of Economic Activities,[8] an adaptation of the United Nations Classification.[9]

A random 10% sample was re-coded blind by an associate researcher to assess the level of missing information, and errors in information transcription of coding. No relevant disagreements were observed with respect to the original coding, and there were no differences between the cases and controls with respect to frequency of errors for occupational data.

No statistically significant differences were observed between bladder cancer cases, hospital controls and population controls with respect to socioeconomic status, educational level, number of different jobs during the professional career, and the length of the interview. For the analysis of occupational exposure, population and hospital controls were pooled together in a single control group.

ANALYSIS

Univariate analysis of the association of bladder cancer with each occupational category was effected by computing the maximum likelihood estimate of relative risk (MLE) for matched data according to the Newton Raphson iterative procedure.[10] The Miettinen formulae[11] were used for exact calculation of confidence limits.

In the simultaneous analysis of specific variables, the potential confounding effect of smoking and/or working in other high risk occupations, as well as the interaction effects, was taken into account using the conditional logistic regression method.[10] Cigarette consumption was included in the model in three categories: smokers, ex-smokers and never-smokers.

All jobs held for at least six months and up to one year prior to diagnosis were analysed according to occupation and industrial activity. For the two controls, the date of diagnosis of the corresponding case was used.

For all large occupational and economic groups, analyses were made separately for men and for women. Those showing an increased risk were further analysed by subgroups. Analysis of subgroups (eg the subgroup of weavers within the textile occupational group) was made by calculating each risk, standardized by other subgroups within this group (eg spinner, dyer, etc) and other high risk occupational groups (manager, mechanic, printer). All occupations and activities that had shown a significantly high risk in previous studies were also analysed.

The reference category varied according to the level of analysis. For large occupational and industrial activity groups, those considered as 'not exposed' had never worked in that occupation or activity. In the analysis of occupational subgroups (eg weavers), those who had never worked in that particular occupation were considered 'not exposed', although they may have held other occupations belonging to the same larger group (eg textile).

Temporal analysis was restricted to males and to the textile and mechanical occupational groups as these were the only occupations with an increased risk of bladder cancer and a large number of exposed subjects.

Attributable risk was calculated according to Miettinen's formula,[12] the synergy index by Rothman's formula,[13] the aetiological fraction attributed to the interaction of occupation and tobacco by the formula proposed by Walker,[14] and the excess risk attributed to this interaction according to Cole and MacMahon's formula.[15] Statistical analyses were performed using a standard statistical package.[16]

RESULTS

Table 1 shows the number of cases and controls, the relative risk (RR), and the confidence limits for each large occupational group. For men, a statistically significant increased risk of bladder cancer was observed for managers, textile workers and assembly and maintenance mechanics. The relative risk for printers (RR = 2.06) was of borderline significance, the lower 95% confidence limit being 1.0. The increased risk for males in the clothing industry was elevated but not statistically significant. For women, textile industry employment is the only occupation for which an increased risk was found; the relative risk is quite high (RR = 6.35) although confidence limits are wide (95% CL:. 1.3–61.6).

Relative risk estimates were only slightly modified (Table 1) after adjustment in the logistic regression model for cigarette consumption and other high risk occupations.

Table 2 shows analyses of high risk occupational groups by subgroups. Within the manager group, the highest risk was observed for company executives and managers. In the textile group, the highest and most statistically significant risk was for the subgroup of weavers, for both men and women. For mechanics, the highest risk was for machine assembly and machine maintenance workers and in graphic arts it was for typesetters and linotypists. Mechanical and textile supervisors and charge hands also presented an increased risk.

The analysis of risk associated with economic activity (Table 3) shows an increased risk for males in the metal production and metalworking industry, the extraction of non-metallic minerals and the textile industry, although only the latter was statistically significant (RR = 1.91; 95% CL: 1.1–3.3). The risk for the textile industry, when measured as an economic activity, is very similar to the results obtained when this is considered as an occupational group. No increase in risk was observed for the chemical, leather, rubber or plastics industries.

Table 4 shows the analysis of time variables for

TABLE 1 *Cases, controls and relative risk by sex. Large occupational groups*

Occupational group	Code	Males CA/CO	Males RR (MLE)	Males CL (95%)	Females CA/CO	Females RR (MLE)	Females CL (95%)
Professionals	01/19	32/70	1.01	0.7–1.5	—	—	—
Managers	20/21	22/28	2.03	1.2–3.5	—	—	—
			(2.04)*	(1.1–3.9)			
Clerical	30/39	93/211	1.08	0.8–1.4	—	—	—
Sales	40/49	73/161	1.03	0.8–1.4	4/16	0.52	0.2–1.1
Service workers	50/59	72/204	0.79	0.6–1.1	22/53	0.87	0.5–1.6
Agric/cattle	60/62	153/363	0.91	0.7–1.1	12/23	1.39	0.6–3.4
Forestry	63	9/20	0.94	0.5–1.8	—	—	—
Hunting/fishing	64	9/25	0.89	0.4–1.7	—	—	—
Miners	71	22/46	1.07	0.7–1.7	—	—	—
Metal processor	72	35/67	1.23	0.8–1.8	—	—	—
Wood, paper	73	10/18	1.25	0.6–2.5	—	—	—
Chemical	74	12/22	1.37	0.7–2.6	—	—	—
Textile workers	75	41/54	1.97	1.2–3.3	11/11	6.35	1.3–61.6
			(1.87)*	(1.1–3.1)		(6.35)	(1.3–30.0)
Food, beverages	77	24/70	0.70	0.5–1.1	—	—	—
Dressmakers	79	11/10	1.75	0.8–3.7	6/12	0.83	0.3–2.2
Leather workers	80	7/18	0.69	0.3–1.5	—	—	—
Furniture, wood	81	12/27	0.95	0.5–1.7	—	—	—
Toolmakers	83	31/87	0.77	0.5–1.1	—	—	—
Mechanics	84	58/84	1.86	1.2–2.8	—	—	—
			(1.79)*	(1.2–2.7)			
Electrical	85	24/49	1.09	0.7–1.6	—	—	—
Plumbers	87	29/66	0.95	0.6–1.4	—	—	—
Glass/ceramics	89	15/37	0.95	0.5–1.6	—	—	—
Rubber/plastics	90	5/13	0.94	0.4–2.3	—	—	—
Printers	92	15/19	2.06	1.0–4.3	—	—	—
			(1.84)*	(0.8–4.1)			
Painters	93	17/38	1.16	0.7–2.0	—	—	—
Others NEC	94	2/9	0.54	0.1–1.6	—	—	—
Construction	95	115/275	0.92	0.7–1.1	—	—	—
Load/unloading	97	51/125	0.96	0.7–1.3	—	—	—
Transport operators	98	45/102	1.08	0.8–1.5	—	—	—
Labourers NEC	99	20/44	1.14	0.7–1.9	—	—	—
Total		438/986			59/127		

* Adjusted for tobacco consumption and exposure to other high risk occupations

TABLE 2 *Cases, controls and relative risk by sex. Occupational subgroups*

Occupational subgroup	Code	Males CA/CO	Males RR (MLE)*	Males CL (95%)	Females CA/CO	Females RR (MLE)*	Females CL (95%)
MANAGERS:							
Company managers and executives	211	23/27	2.09	1.1–4.1	—	—	—
TEXTILE:							
Supervisors and foremen	700.70	14/12	2.45	0.9–6.4	—	—	—
Fiber	751	6/14	1.50	0.5–4.5	—	—	—
Spinners	752	6/11	0.94	0.3–2.9	3/5	3.72	0.4–32.1
Loom operators	753	2/2	1.36	0.2–11.6	—	—	—
Weavers	754/755	10/7	3.52	1.3–9.3	9/6	21.15	1.5–297.9
Dyers	756	11/17	1.29	0.5–3.1	1/2	0.34	0.1–7.7
Others	758/759	3/4	4.28	0.6–29.4	1/1	1.29	0.2–86.9
MECHANICS:							
Supervisors and foremen	700.50	9/9	2.39	0.7–8.3	—	—	—
Machine assembler, maintenance	841	19/18	2.61	0.7–10.0	—	—	—
Precision mechanics	842	4/6	—	—	—	—	—
Motor mechanics	843	14/29	1.09	0.4–2.8	—	—	—
Plane mechanics	844	3/1	—	—	—	—	—
Others	849	18/34	1.17	0.5–3.0	—	—	—
GRAPHIC ARTS:							
Typesetters, linotypists	921	9/10	2.02	0.5–7.5	—	—	—
Printers	922	1/2	1.41	0.0–117.6	—	—	—
Engravers	924	1/6	0.35	0.0–3.2	—	—	—
Photoengravers	925	1/1	—	—	—	—	—
Photographic laboratory	927	1/0	—	—	—	—	—
Others	929	2/2	—	—	—	—	—

* Conditional logistic regression analysis, adjusting for cigarette consumption, exposure to other high risk groups and exposure to other subgroups within the same occupational group

mechanics and textile workers. In the textile industry, the highest risk appears for those who began working before the age of 25 and prior to 1960, who were employed for a period of more than five years, and after a long latency period (30 years or more). The latency period observed varied from 10 to 65 years, with a mean of 41 years. In mechanical occupations on the other hand, the greatest risk was observed for those who began working after the age of 25 and later than 1960. Length of time since first exposure and duration of exposure did not appear to modify the risk. The latency period observed varied from 3 to 64 years, with a mean of 37 years.

The results of the analyses of the joint effect of occupational exposure and cigarette smoking are shown in Table 5. The relative risk for those who have never smoked but who have been occupationally exposed was 1.13 (95% CL: 0.39–3.28) relative to those who neither smoked nor were occupationally exposed. For smokers with no occupational exposure, the risk was 4.35 (2.75–7.12) and for smokers who have also been occupationally exposed (in the textile, mechanical and/or the graphic industry), it was 7.82 (95% CL: 4.38–13.98). These estimates of the RR are compatible with a multiplicative effect of both factors.

DISCUSSION

Occupational Groups

The results of the present study confirm our previous observation[4,5] that exposure occurring in the textile industry is one of the main occupational risk factors for bladder cancer in Spain. This association has been demonstrated in other studies[17–19] and is probably due to the use of carcinogenic dyes derived from aromatic amines. Although in the US Silverman[20] and Schoenberg[21] did not find any association, only a very small number of cases and controls included in their study had been employed in the textile industry.

Within the textile industry we observed the greatest risk for those employed as weavers, especially women. Anthony and Thomas[17] also reported a high relative risk of 6.5 for weavers.

Two of the regions included in our study have since the end of the last century had a high concentration of textile factories, employing 20–30% of the active population. One of these areas is Mataró county,

TABLE 3 *Cases, controls and relative risk by sex. Large economic activity groups*

Activity group	Code	Males CA/CO	Males RR (MLE)	Males CL (95%)	Females CA/CO	Females RR (MLE)	Females CL (95%)
Agriculture	01	140/324	0.93	0.7–1.1	12/22	1.37	0.6–3.0
Cattle	02	44/83	1.29	0.9–1.8	—	—	—
Forestry	05	11/18	1.25	0.6–2.4	—	—	—
Fishing	06	9/31	0.70	0.4–1.3	—	—	—
Coal mining	11	10/18	1.38	0.6–3.1	—	—	—
Prod/distrib of gas/electricity	15	10/24	1.12	0.6–2.1	—	—	—
Metal mining	21	12/31	0.85	0.5–1.5	—	—	—
Fabricated metal products	22	20/38	1.64	0.9–2.9	—	—	—
			(1.68)*	(0.8–3.4)			
Non-metallic mineral mining	23	9/14	1.80	0.8–3.8	—	—	—
			(1.68)*	(0.7–4.3)			
Non-metallic mineral industry	24	27/75	0.87	0.6–1.3	—	—	—
Chemical industry	25	21/47	1.06	0.6–1.8	—	—	—
Metallic manufacture	31	57/143	0.84	0.6–1.1	—	—	—
Machinery manufacture	32	25/58	0.96	0.6–1.5	—	—	—
Manufacture of electric goods	34	20/45	0.83	0.5–1.4	—	—	—
Electronics industry	35	2/9	0.44	0.1–1.5	—	—	—
Car manufacture	36	8/37	0.52	0.2–1.1	—	—	—
Boat manufacture	37	30/70	0.97	0.6–1.5	—	—	—
Transport material	38	11/75	0.87	0.6–1.3	—	—	—
Optical industry	39	4/11	0.82	0.2–2.6	—	—	—
Food, beverages	41/42	42/112	0.79	0.5–1.1	3/9	0.79	0.2–2.6
Textile industry	43	45/67	1.91	1.1–3.3	11/13	3.31	0.9–15.0
			(2.02)*	(1.2–3.4)		(3.31)*	(1.0–10.9)
Leather industry	44	4/9	1.11	0.2–5.1	—	—	—
Footwear clothing	45	15/25	1.09	0.5–2.1	6/7	1.38	0.3–5.9
Wood, cork	46	29/68	1.04	0.6–1.7	—	—	—
Paper, graphics	47	19/48	0.92	0.5–1.6	—	—	—
Rubber, plastic	48	6/18	0.73	0.3–1.9	—	—	—
Other industry	49	9/13	1.58	0.6–3.8	—	—	—
Construction	50	140/306	0.87	0.7–1.1	—	—	—
Sales	61/64	72/189	1.16	0.9–1.5	4/13	0.62	0.2–1.6
Restaurants, hotels	65/66	36/67	0.70	0.5–1.0	—	—	—
Repairs	67	22/50	1.04	0.6–1.7	—	—	—
Transport	71/75	70/139	1.02	0.8–1.3	—	—	—
Communication	76	3/11	2.10	0.8–5.5	—	—	—
Financial services	81/99	98/234	1.01	0.8–1.3	22/53	0.86	0.4–1.7
Total		438/986			59/127		

* Adjusted for cigarette consumption and exposure to other high risk activities

specializing in the production of cotton goods; the other is Terrassa, which mainly concentrates on wool-based products. The overall risk is similar although there are some differences: in Mataró the highest risk and the most prevalent exposure among cases is observed in those employed in the weaving sector; in Terrassa, on the other hand, the most prevalent exposure corresponds to the dying and spinning of wool products.

Machine operators and various occupations in the metal industry are exposed to cutting oils used as coolants, rust inhibitors and lubricants which contain beta-naphthylamine and nitrosamines.[22] Previous studies have reported high relative risks for die- and tool-makers,[23] and for lathe operators.[19] Decouflé, however, did not find any increase in risk in a group of workers exposed to cutting oils.[24] In our study, we observed no association between these occupations and bladder cancer even though there was a reasonable number of study subjects holding these jobs (31 cases, 87 controls). On the other hand, we did observe a relative risk of 1.86 (95% CL: 1.2–2.8) for machinery adjusters, assemblers and mechanics. These results are similar to those obtained by Silverman in Detroit,[20] who did not find any increased risk for die- and tool-makers, but found a risk of 2.1 for machinery operators in the automobile industry. Further studies may clarify these inconsistencies.

TABLE 4 *Number of cases and controls and relative risk according to time variables in the textile and mechanical occupational group*

	Textile CA/CO	Textile RR (MLE)	Textile CL-95%	Mechanics CA/CO	Mechanics RR (MLE)	Mechanics CL-95%
Age at first exposure (years)						
<19	23/24	2.42	1.25–4.66	27/46	1.65	0.95–2.27
20–25	5/3	3.29	0.62–17.35	9/16	1.24	0.53–2.90
>25	13/27	1.46	0.69–3.08	22/22	2.59	1.32–5.10
Year of first exposure						
<1950	27/32	2.26	1.22–4.17	37/57	1.77	1.09–2.87
1950–1960	9/9	2.48	0.91–6.73	9/15	1.52	0.60–3.83
>1960	5/13	1.02	0.31–3.38	12/12	2.15	0.89–5.17
Duration (years)						
<5	10/15	1.49	0.62–3.58	14/21	2.23	1.02–4.90
5–10	9/9	2.86	1.04–7.90	8/19	0.93	0.38–2.23
>10	22/30	2.13	1.12–4.05	36/44	2.07	1.24–3.44
Latency period (years)						
<31	10/20	1.40	0.57–3.41	19/20	2.48	1.25–4.91
31–45	15/14	2.35	1.03–5.34	20/40	1.20	0.67–2.16
>45	16/20	2.18	1.01–4.74	19/24	2.49	1.23–5.02

Reference category = Not exposed

TABLE 5 *Number of cases and controls and relative risk according to cigarette consumption and simultaneous exposure to high risk occupations. (Textile, mechanical and printers). Males*

Cigarette consumption	Occupational exposure	Cases	Controls	RR (MLE)*	CL 95%
Never	No	65	278	1	
Ex-smoker	No	64	213	2.54	1.46–4.40
Smoker	No	252	460	4.35	2.65–7.12
Never	Yes	16	47	1.13	0.39–3.28
Ex-smoker	Yes	23	27	9.26	4.12–20.81
Smoker	Yes	77	88	7.82	4.38–13.98
Total		497	1113		

* Conditional logistic regression for each combination of simultaneous exposure to cigarettes and occupational risk in relation to no occupational exposure and never-smoker

When the analysis was restricted to Viscaya (the area of Spain with the highest concentration of blast furnaces for the iron and steel industry), we observed a relative risk of 1.92 (95% CL: 1.0–3.7 based on 21 cases and 32 controls. Of this group, 7 cases and 16 controls worked in furnaces (RR = 1.70, 95% CL: 0.6–4.8) and 4 cases and 4 controls in rolling mills (RR = 1.83, CL: 0.4–9.0). The possibility of an increased risk in these occupations is also supported by the risk observed for the production and metalworking industries although it is not statistically significant (Table 3).

Previous studies[23,25,26] have already reported a high relative risk of printshop workers. In occupations with probable exposure to printing inks we have observed a risk of 2.06 (95% CL: 1.0–4.3) which is on the border of statistical significance.

The surprisingly high relative risk observed for managers does not disappear when standardized for cigarette consumption. Neither can this high risk be explained by previous exposures, since most of the subjects had been employed only in the service sector. It is possible that this risk is the result of an association with other factors, or simply a chance result due to the large number of occupations analysed.

Other occupations exposed to aromatic amines or aromatic polycyclic hydrocarbon, for which some association with bladder cancer has been reported are those of cork and tyre manufacturing,[18,19,27,28] leather industry,[18,24,28] dyestuffs,[18,19,29] coal gas[30] and aluminium workers.[31] Our negative results for these occupations may be explained by their near absence in the geographical areas covered by our study.

Other occupational groups found to be at increased risk in previous studies are truck drivers[20] and workers exposed to car and diesel exhausts.[27] Our study includes 42 cases and 102 controls who had worked as transport drivers. The relative risk was 1.08 (95% CL: 0.8–1.5). The subgroup of motor vehicle drivers, with 31 cases and 64 controls, shows a relative risk of 1.13 (95% CL: 0.7–1.8).

Time Variables

The risk of bladder cancer according to age at first exposure to the occupation has shown contradictory results. Case[29] observed an increase in risk with increasing age, whereas Hoover and Cole[32] reported a higher risk for those whose occupational exposure started before the age of 25. One of the possible explanations for these differences was the fact that the two studies included different occupations at increased risk: dye workers in England and rubber and leather workers in Boston. Schulte[33] in a cohort of workers exposed to aromatic amines, points out that there is no excess of risk for exposure beginning after the age of 25.

Our results support the hypothesis that the risk is modified by age and that it depends on the type of work. In the textile industry we observed a higher risk for those exposed before the age of 25, while for mechanics it was highest for those who started after 25.

Risk differences related to age at first exposure could indicate differences in biological susceptibility or be the real expression of the induction period. They could also reflect changes in the production processes and/or the level of exposure. Age, duration and latency period, however, are often strongly correlated, and it is sometimes difficult to separate these effects.

The effect of age persists, however, when the data are analysed separately in two strata by duration of exposure, higher or lower than 10 years (Table 6). In the textile industry, the risk is higher for those who began younger than 25, independently of the duration. For mechanics, on the other hand, the higher risk persisted for those who were first employed as mechanics after the age of 25, regardless of the duration of the occupational exposure.

Hoover and Cole[32] observed that the highest risk, for occupational exposures appeared after a latency of 41 to 50 years. They note, however, that an increase in the duration of exposure (more than 10 years) reduced the latency period. We observed the same phenomenon for exposure to textiles (Table 7). With less than 10 years' exposure, the highest risk appears after a latency period of more than 40 years, but it decreases with increasing exposure time. This effect was not observed among mechanics.

TABLE 6 *Relative risk and 95% confidence limits according to age at first exposure and duration of the occupation in the textile and mechanical occupational groups*

Duration of the occupation (years)	Age at first exposure (years) $\leqslant 25$	>25
$\leqslant 10$		
Textile	3.24	0.87
	(1.39–7.50)	(0.25–2.99)
Mechanical	1.04	3.36
	(0.51–2.14)	(1.22–9.32)
>10		
Textile	2.14	1.52
	(0.96–4.72)	(0.60–3.82)
Mechanical	1.90	2.73
	(1.05–3.41)	(1.14–6.53)

Reference category = not exposed

The age at start of and the duration of employment in a particular occupation are not necessarily identical to age and duration of exposure. Case-control studies based on occupational history do not allow precise evaluation of exposure to particular chemical substances or of the periods involved.[34] For this reason, results from the analysis of time variables must be considered very cautiously.

Interaction of Smoking and Occupation

Our study confirms previous observations on the plausibility of a multiplicative interaction effect of cigarette smoking and occupational exposure to aromatic amines.[5,26,35,36]

The index of synergy between smoking and occupational exposures computed on the present data was 1.96 and the excess risk due to the interaction was estimated

TABLE 7 *Relative risk and 95% confidence limits according to the latency period and the duration of the occupation in textile and mechanical occupational groups*

Duration of the occupation (years)	Latency period (years) $\leqslant 40$	>40
$\leqslant 10$		
Textile	1.01	4.05
	(0.37–2.80)	(1.51–10.86)
Mechanical	1.71	1.36
	(0.78–3.72)	(0.60–3.10)
>10		
Textile	2.42	1.54
	(0.96–6.10)	(0.66–3.60)
Mechanical	2.13	2.07
	(1.15–3.94)	(0.91–4.72)

Reference category = not exposed

as 3.34. The calculation of the aetiological fraction attributed to the interaction indicates that 50% of the aetiological fraction of joint exposure to smoking and occupation is due to synergy between the two factors.

Analysis of the simultaneous effect of smoking and occupation (Table 5) also shows that the effect of smoking cessation varies depending on the occupational exposure. For cigarette smokers who have had no occupational exposure, ex-smokers who gave up smoking at least five years previously have a 50% reduction in risk if they have not been occupationally exposed. For those who have had occupational exposure, giving up smoking does not reduce the risk. It is as if the risk from occupational exposure were irreversible. Hoover and Cole have already pointed out the possibility that certain occupational carcinogens act both as initiators and promoters of bladder cancer.[32]

Our data estimates the proportion of bladder cancer cases attributable to occupational exposures at 12%. This is mainly accounted for by employment in the textile, mechanical and graphic industries. Our estimate is close to some of the highest values observed in previous studies[1] and indicates that one in eight cases of bladder cancer that occurred in the source population could have been avoided by controlling occupational exposure.

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