Smoking, occupational exposure to rubber, and lung cancer

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ABSTRACT A cohort of 1624 employees (957 men, 667 women) in a rubber factory in Shanghai have been followed up since 1972 and their 12 year mortality experience is presented. The relative risk of lung cancer for smokers was 8.5 for men and 11.4 for women and for rubber workers exposed to curing agents or talc powder 3.2 for men and 4.6 for women.

Although many researchers have found that lung cancer is positively related to various jobs within the rubber industry,¹ the effect of smoking on lung cancer and the interaction between smoking and exposure to rubber have not yet been reported. These questions have been explored by following up a cohort of 1624 rubber workers in Shanghai from 1 December 1972 to 30 November 1984.

Material and methods

SUBJECTS

A total of 1624 rubber workers (957 men, 667 women) in the Xuhui district of Shanghai who entered a screening programme for coronary heart disease in 1972 were included in the study. Thirty items such as smoking habit, drinking habit, and information on work history were obtained from the records of the screening programme. Records of subjects who took part in the screening programme were checked in 1982 and 1984 and the causes of death from death certificates classified by ICD-9². Eighty seven men and one woman were lost to follow up and the rate of follow up was 95% (91% for men, 99% for women).

ANALYSIS

Direct and indirect standardisation were used to calculate standard death rates and SMRs.³ The age distribution of the general population in Xuhui district with their specific cause of death from 1974 to 1984 was used as the standard. The data were stratified by smoking and jobs within the rubber plant. The Mantel-Haenszel method for follow up studies was used to analyse the effects of smoking and exposure to rubber on the risk of lung cancer.⁴ Additive and

multiplicative models were used to evaluate possible interaction effects.⁵

The equation⁶ used to test the significance of a difference of SMR from 100 is shown as follows:

$$\chi^2 = \frac{(|\text{Obs} - \text{Exp}| - 1/2)^2}{\text{Exp}}, n' = 1$$

Results

Table 1 shows the 12 year mortality experience of 1624 rubber workers (including both active and retired). The death rate for all causes in rubber workers was less than that in the general population, whereas the mortality for all malignant neoplasms was close to that in the general population. The SMR for lung cancer was the highest among the five main cancers. The attributable risk (rate difference) for lung cancer in rubber workers was 15/100 000 person-years for men and 10/100 000 person-years for women, compared with the average death rate of lung cancer in Xuhui district from 1974 to 1984.

The death rate from lung cancer in rubber workers with reference to the type of jobs was also analysed. The rubber workers were divided into five subgroups: (1) curing; (2) the inner tube of tyre; (3) raw material handling, weighing, mixing, extruding, and calendering; (4) component assembly and building; and (5) general service in the factory. The SMRs for lung cancer for curing workers were 286 for both sexes (263 for men, 500 for women) and those for inner tyre tube workers were 375 for both sexes (333 for men, 500 for women). The SMRs for lung cancer for curing and inner tube workers were higher than those for the other three groups (table 2).

The lung cancer death rate in rubber workers with reference to cigarette smoking was explored. The rate

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Table 1 Observed and expected number of deaths, SMR, and standard deaths rates (/100 000/year) in rubber workers in Shanghai by cause of death (1972-84)

ICD-9	Cause of death	Both sexes				Men				Women			
		Obs	Exp	SMR	Rate	Obs	Exp	SMR	Rate	Obs	Exp	SMR	Rate
001-999	All causes	163	191.6	85	463	117	132.9	88	472	46	58.7	78	295
140-208	Neoplasms	66	65.9	100	157	48	48.2	100	183	18	17.7	102	106
162	Lung cancer	20	15.1	133	49	16	12.1	132	60	4	3.0	132	31
151	Cancer of stomach	13	14.0	93	31	12	11.1	109	46	1	2.9	35	5
155	Liver cancer	10	10.1	99	23	8	8.2	98	32	2	1.9	105	9
153	Cancer of colon	4	4.6	87	10	2	2.8	71	7	2	1.4	140	14
150	Cancer of oesophagus	4	6.2	65	10	3	5.0	61	12	1	1.2	80	6

Table 2 Observed and expected number of deaths and SMR of lung cancer of rubber workers in Shanghai from 1972 to 1984 by type of job

Type of job	Both sexes			Men			Women		
	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR
(i) Curing	6	2.1	286*	5	1.9	263	1	0.2	500
(ii) Inner tyre tube	3	0.8	375	2	0.6	333	1	0.2	500
(iii) Raw material handling, etc	3	2.9	104	3	2.7	111	0	0.2	0
(iv) Component assembly, etc	0	1.6	0	0	1.1	0	0	0.5	0
(v) General service	8	7.7	104	6	5.8	103	2	1.9	105

*p < 0.05.

of correspondence of the daily averages of cigarette smoking between 1972 and 1982 was 89% (table 3). The average proportions of smokers from 1972 to 1984 are 63% for male workers and 9% for female workers, which are higher than those in the general population in Xuhui district in 1983 (46% for men, 5% for women, unpublished data). The excess proportions of smokers in the rubber factory compared with the general population were 39% for men, 69% for women, and 56% for both sexes; the excess proportions for lung cancer mortality were 32% for men, 50% for women, and 47% for both sexes (table 4). Although the proportion of smokers in male curing and inner tube workers was similar to that in other male workers (63% compared with 64% for other workers), the proportion of heavy smokers (> 10/day) in curing and inner tube workers was 51%, which was higher than that in other workers (41%). The popula-

tion attributable risk (PAR) of lung cancer in rubber workers who smoked was 83% for men and 48% for women (Shanghai: 81% for men, 19% for women, unpublished data). The SMRs for lung cancer in heavy smokers of both sexes were the highest among the three smoking groups and were significantly raised. There was a dose response relation between average daily cigarette smoking and lung cancer SMR (table 5).

Rubber workers were divided into two groups: smokers and non-smokers and the crude relative risk of lung cancer for smokers was 8.7 for men and 10.3 for women. To calculate the Mantel-Haenszel relative risk (RR), these workers were divided into four subgroups by smoking habit (smoker and non-smoker) and exposure to curing agents or inner tubes (yes or no). When the data were stratified by occupational exposure (to curing agents or inner

Table 3 Rate of correspondence* of daily average of smoking between 1972 and 1982 in rubber workers†

Results of survey in 1972	Results of survey in 1982 (No of subjects)				Total
	Non-smoking	1-10 cig/day	11-20 cig/day	> 20 cig/day	
Non-smoking	750	37	3	1	791
1-10 cig/day	17	158	64	0	239
11-20 cig/day	8	14	332	17	371
> 20 cig/day	1	0	3	69	73
Total	776	209	402	87	1474

*Rate of correspondence (%) = $\frac{(750 + 158 + 332 + 69)}{1474} \times 100 = 89\%$

†Rate of follow up from 1972 to 1982 was 91%.

Table 4 Proportion of smokers and lung cancer mortality for rubber workers and general population of Xuhui district in Shanghai, 1972–84

Sex	Person-years	Person-years of smoking	Proportion of smokers (%)		Excess (%)	Mortality of lung cancer (/100 000/year)		
			Rubber workers	Xuhui area†		Rubber workers	Xuhui area‡	Excess (%)*
Male	10053	6373.5	63	46	39	60	46	32
Female	7562	668.0	9	5	69	31	21	50
Both sexes	17615	7041.5	40	26	56	49	33	47

*Equation for calculating excess proportion is as follows:
Excess proportion (%) = $\frac{\text{rubber workers} - \text{Xuhui area}}{\text{Xuhui area}} \times 100$.

†Proportion of smokers for Xuhui area was supplied by Xuhui Anti-Epidemic Station from a sample survey (10% random sample from all population) in 1983 (unpublished data).
‡Mortality of lung cancer in Xuhui district 1974–84.

Table 5 Observed and expected number of deaths and SMR for lung cancer of rubber workers in Shanghai, 1972–84 by smoking and sex

Smoking status	Both sexes			Men			Women		
	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR
Non-smoking	3	6.8	44	1	4.2	24	2	2.6	77
1–10 cig/day	1	1.9	53	1	1.7	59	0	0.2	0
> 10 cig/day	16	6.4	250**	14	6.2	226**	2	0.2	1018**

**p < 0.01.

tubes), the RR of lung cancer for smokers was 8.5 for men (1.6–45.2) and 11.4 for women (2.4–53.5) (table 6).

The crude relative risk of lung cancer for occupational exposure (to curing agents or inner tubes) was 3.3 for men and 4.0 for women. When the effect of smoking was controlled (stratified by smoking habit), the RR for curing agent or inner tube exposure was 3.2 (1.3–8.2) for men and 4.6 (0.8–27.9) for women (table 7).

Additive and multiplicative models were used to evaluate the interaction between smoking and occupational exposure on lung cancer. Although the additive interaction term was 27/100 000 person-years, this was not statistically significant ($z = 0.33$, $p > 0.05$) and also a negative multiplicative interaction was found (table 8).

Discussion

In the present study an excess of lung cancer in Shanghai rubber workers was found. The age standard death rate of lung cancer for rubber workers was higher than that for the general population in the same district and during the same period, and the SMR for lung cancer was the highest among all causes of death. Mancuso noted an excess of lung cancer in Ohio rubber workers in 1949.⁷ Since then, there have been similar results in the United States, Britain, and Finland.^{8–10}

Our study also shows a significant excess of deaths from lung cancer, particularly in those who worked in the curing workshop and a high but not statistically significant excess in those in the inner tube workshop. British investigators reported an excess of lung cancer among workers in tyre manufacture, particularly those engaged in the process of curing.⁹ Some epidemiologists in the United States also reported similar results in the curing workshop.^{11–13} The agent responsible for the excess of lung cancer is still obscure. In the curing workshop goods are sprayed with a solvent based lubricant before curing. The curing process itself generates condensed volatiles, vapours, and gases with unknown nature. In addition to curing agents, another possible cancer causing agent in the rubber industry is talc powder. In the inner tube workshop talc powder is used to dust the inner tyre tube. Kleinfeld and colleagues found that the proportional mortality rate for lung cancer in workers exposed to commercial talc dust was four times that of

Table 6 Stratifying on the degree of exposure to curing agents and inner tubes to assess the association between smoking and lung cancer

Sex	RR _{crude}	RR	95% CI for RR
Male	8.7*	8.5*	1.6–45.2
Female	10.3**	11.4**	2.4–53.5

*p < 0.05; **p < 0.01.

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Table 7 Stratifying on the degree of smoking to assess the association between exposure to curing agents and inner tubes and lung cancer

Sex	RR _{crude}	RR	95% CI for RR
Male	3.3*	3.2*	1.3- 8.2
Female	4.0	4.6	0.8-28.0

*p < 0.05.

the general population.¹⁴ Thomas and Stewart reported that workers exposed to talc had a significant 2.5-fold excess risk of lung cancer.¹⁵ In our study the RR of lung cancer in workers exposed to curing and talc was 3.2 for men and 4.6 for women after the effect of smoking was controlled.

In the evaluation of lung cancer mortality the possible influence of cigarette smoking must be considered. In the present study the proportion of smokers among the rubber workers was higher than in the general population and the proportion of heavy smokers in curing and inner tyre tube workers was higher than in the other three groups, which was probably responsible for the excess of lung cancer in rubber workers, especially for workers in curing and inner tube workshop. There was a dose response relation between the SMR for lung cancer and daily averages of cigarette smoking. When the effect of exposure to rubber was controlled, the RR of lung cancer for smokers was more than eight and statistically significant. Doll and Hill reported that the relative risk of lung cancer in smokers was 12.9.¹⁶ The results of our research show a strong association between cigarette smoking and lung cancer and suggest that there is an urgent need to adopt effective measures against smoking in rubber workers.

In other industrial studies of lung cancer cigarette smoking was found to interact with certain occupational exposure.¹⁷ Selikoff and colleagues¹⁸ and Saracci¹⁹ analysed the epidemiological evidence on the asbestos-smoking interaction. Lednar and colleagues reported that smoking and rubber occupational exposure interact for pulmonary disability.²⁰ In our data, although the additive interaction term was 27/100 000 person-years, this was not statistically significant.

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Table 8 Analysis of interaction between smoking and occupational exposure to curing agents and inner tubes on deaths from lung cancer

Smoking status	Age adjusted mortality rate (/100 000/year)		Relative risk		Attributable risk (/100 000/year)	
	Non-exposure	Exposure*	Non-exposure	Exposure	Non-exposure	Exposure
Non-smoking	6	50	1.0	8.3	0	44
Smoking	98	169	16.3	28.2	92	163

*Z = 0.33, p ≥ 0.05.

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