PostScript

LETTER

Cancer and non-cancer mortality in a cohort of recent entrants (1981-2000) to the German rubber industry

Working in the rubber industry is associated with increased cancer risks, particularly for cancers of the lung, larynx, urinary bladder and leukaemia.¹ Most epidemiological studies, however, still reflect working conditions back to the 1940s. As occupational exposures were lowered considerably since the late 1970s, prospective health surveillance is warranted to assess the effectiveness of exposure control.

Methods

The cohort included all blue-collar workers of 13 participating rubber manufacturing companies in western Germany who were hired after 1 January 1981 and worked for at least 1 year until the end of follow-up. Follow-up started on 1 January 1982 and ended on 31 December 2000, but was censored at the age of 85 years.

The vital status was ascertained via population registries. Death certificates were

requested from community health departments and underlying causes of death were coded by professional nosologists according to the ninth revision of the International Classification of Diseases (ICD-9).

The mortality experience of the cohort was compared with the mortality of the corresponding population of western Germany. Standardised mortality ratios (SMRs) and exact 95% confidence intervals were calculated stratified by gender and nationality and standardised by calendar year and 5-year age groups using the PAMCOMP software.² A lag period of 10 years was applied to SMR analysis of all-cause and all-cancer mortality—that is, the first 10 years after starting work were ignored.

Results

The cohort included 8210 male and 1387 female German and 2476 male and 229 female non-German blue-collar workers. Vital status ascertainment was almost complete (98% for German; 94% non-German). Death certificates were obtained for 90% of the German and 67% of the non-German decedents; only four cancer deaths were observed among non-German decedents.

Among German cohort members 25% have been employed for more than 10 years in the rubber industry and 47% have been hired between 1981 and 1989. The majority of deaths have occurred in the last five years of follow-up.

Among German men the decreased mortality (table 1) was mainly due to lower mortality from diseases of the circulatory system and cancer. For women the all-cause mortality and all-cancer mortality was higher than expected.

Among male German rubber workers mortality from cancers of the oral cavity and pharynx was increased based on a total of three cases, and lung cancer mortality was lower than expected. Among female German rubber workers increased SMRs on the basis of only one or two deaths were observed for several cancer sites, including stomach, lung and leukaemia. No death from bladder cancer was observed in the entire cohort with 0.3 expected deaths for German men.

Discussion

We observed a healthy worker effect among German male rubber workers and increased all-cause and all-cancer mortality among female rubber workers. With lagging, the

Table 1 Number of observed deaths (Obs) and standardised mortality ratios with 95% confidence intervals among male German (n=8210) and female German (n=1387) rubber workers between 1981 and 2000 by cause of death

Cause of deaths	ICD-9	Male		Female	
		Obs	SMR* (95% CI)	Obs	SMR† (95% CI)
All causes	000-999	100	84 (68 to 102)	16	134 (77 to 218)
All causes (with 10-year lag)	000-999	26	74 (48 to 108)	6	145 (53 to 315)
All cancer	140-208	15	69 (39 to 114)	5	111 (36 to 259)
All cancer (with 10-year lag)	140-208	8	99 (43 to 195)	3	172 (35 to 502)
Cancer sites					
Lip or oral cavity or pharynx	140-149	3	191 (39 to 559)	0	—
Oral cavity	141, 143-145	1	159 (4 to 886)	0	—
Pharynx	146-149	2	223 (27 to 806)	0	—
Digestive organs or peritoneum	150-159	4	69 (19 to 177)	2	228 (28 to 825)
Stomach	151	0	—	1	465 (12 to 2590)
Colon	153	2	162 (20 to 587)	0	—
Rectum	154	1	151 (4 to 839)	0	—
Liver or gallbladder	155-156	0	—	1	940 (24 to 5237)
Pancreas	157	1	106 (3 to 593)	0	—
Respiratory and intrathoracic organs	160-165	4	77 (21 to 197)	1	217 (5 to 1208)
Trachea or bronchus or lung	162	4	88 (24 to 225)	1	235 (6 to 1307)
Breast	174	0	—	0	—
Testis	186	1	172 (4 to 957)	0	—
Brain	191-192	0	—	0	—
Without specification of site	199	1	84 (2 to 468)	1	538 (14 to 2996)
Lymphatic and haematopoietic tissue	200-208	2	71 (9 to 256)	1	247 (6 to 1378)
Lymphatic system	200-203	2	140 (17 to 507)	0	—
Leukaemia	204-208	0	—	1	472 (12 to 2629)
Other neoplasms	210-239	0	—	1	1000 (25 to 5570)
Non-cancer					
Diabetes mellitus	250	1	86 (2 to 477)	0	—
Diseases of the circulatory system	390-459	12	59 (31 to 104)	2	103 (13 to 374)
Ischaemic heart disease	410-414	5	55 (18 to 128)	2	356 (43 to 1285)
Cerebrovascular disease	430-438	2	66 (8 to 238)	0	—
Diseases of the respiratory system	460-519	3	106 (22 to 311)	0	—
Chronic obstructive pulmonary disease	490-496	2	137 (17 to 493)	0	—
Diseases of the digestive system	520-579	5	64 (21 to 149)	2	244 (30 to 880)
Chronic liver disease	571	2	35 (4 to 126)	2	343 (41 to 1238)
Injury and poisoning	800-999	33	82 (56 to 115)	3	138 (29 to 404)

*SMR based on the male German population of western Germany as reference.

†SMR based on female German population of western Germany as reference.

healthy worker effect for cancer-related deaths was diminished. Based on small numbers statistically non-significant increases in mortality from cancers of the oral cavity, pharynx, lung, stomach and leukaemia among men or women were noted. The results were not consistent across gender.

The cohort is reasonably large. Nevertheless, the inception cohort design, imposed by the goal to study working conditions in the modern rubber industry, the maximum follow-up of 20 years and the hiring of predominantly young workers into the rubber industry limited the statistical precision.

The SMRs are not adjusted for potential confounders such as tobacco smoking and alcohol consumption. Among men, decreased mortality from lung cancer and chronic liver disease argue against strong confounding. Among women mortality from lung cancer and chronic liver disease was increased and confounding cannot be ruled out. Conversely, both diseases may also be caused by occupational exposures in the rubber industry^{3,4} and smoking is only a moderate risk factor for stomach cancer and leukaemia.

The observed overall pattern of increased cancer-specific SMRs is consistent with our previously reported findings among rubber workers employed in earlier periods³⁻⁵ and with findings from epidemiological studies among rubber workers in other countries.¹ Only one other study has investigated carcinogenic risks in the modern rubber industry.⁶ Interestingly, the only statistically significant increase in mortality was noted for cancer of the testis, which was also increased in our cohort. Yet, the results for incidence of testicular cancer in the British cohort did not support the mortality findings. Due to registration deficits in Germany, the investigation of cancer incidence in our cohort is not feasible.

Conclusions

The cohort is reasonably large but still too young to provide conclusive evidence. Increased cancer risks are consistent with previous results among German rubber workers employed in earlier periods. Pooled analyses of ongoing cohort studies in the modern rubber industry are needed to allow for a robust interpretation.

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*Professor Stephan Weiland unexpectedly died earlier this year. We lost a great friend and excellent scientist. We miss him.

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BOOK REVIEW

Inhalation toxicology

H Salem, S H Katz. Taylor and Francis, 2006, £109. ISBN 0-8493-4049-7

This is a big book that tells you a lot about inhalation toxicology. The editors clearly intend it to be a definitive work and it is aimed both at practising inhalation toxicologists and the "aspiring student". As a reference work for the professional it succeeds well; of its value as a textbook for students I am less certain. About 70 authors have contributed, and there are 40 chapters of varying length. Some deal with the theoretical aspects of the subject, some with regulatory matters and others with compounds or groups of compounds. It is not possible to discuss more than a few chapters in detail.

The first section deals with "Methods and Measurements". The second, confusingly, deals with "Methods" again. No systematic approach seems to have been taken. Chapter 5 for example, provides an interesting account of the rather arcane subject of vapour exposure to

the organophosphorus compound VX. This is fascinating for those, like the reviewer, with an interest in CW agent toxicology. But we are not told why this is important: who is at risk? The chapter discusses Haber's Rule, an important concept, and uses VX as an example of deviation from the rule. A full discussion, from a more general standpoint, early in the book would be useful as this topic comes up again and again in later chapters. Animal models are clearly important and Brown and colleagues have contributed a valuable account of a large animal model. Phosgene is used as an example of a compound that can be studied using such a model. I enjoyed reading this: the inclusion of detailed physiological methods in a toxicology study is encouraging and the authors have provided results which are difficult to find elsewhere, though the latter parts of the chapter read more like a research paper than a textbook account. The provision of information of the advantages and disadvantages of large animal models is, however, limited. Chapter 8 returns to Haber's Rule with force: a range of models is discussed. This is excellent but surely it should have appeared earlier in the book. Levin and Kuligowski have written a valuable chapter on the toxicology of fire and smoke. This discusses the "N-Gas" model but no clear link with the discussion of models in chapter 8 is provided. In the second part of the book, "Methods", Calabrese discusses hormesis (is this a method?), and detailed accounts of the toxicology of, for example, riot control agents and CW compounds are provided. The editors may have regarded these as providing examples of specific methods—I was unconvinced. In the third section Ballantyne and Salem have contributed a magisterial account of the toxicology of cyanides. This runs to about 90 pages and is exhaustively referenced: a quick count suggests about 500 citations; one might wonder what of importance has not been listed! McGrath, on the other hand deals with carbon monoxide rather briefly and provides no discussion of the possible long-term effects of exposure to subsymptomatic concentrations. Toxins and bio-aerosols are dealt with in the final section. Ricin and botulinum toxin command chapters of only about 10 pages—very short in comparison with other chapters. As far as I can see, no discussion of the inhalation toxicology of air pollutants is provided—a significant omission. Also, the fast growing field of nano-particle toxicology is not included. This is a pity as a proper discussion of methods for generating nano-particle aerosols and of the peculiar properties of these substances would be useful at present.

In conclusion: a big book with many important contributions, some unique and reflecting the special interests of the authors. However, the organisation and balance could be improved. All professional inhalation toxicologists will want a copy: the price, by today's standards, is very reasonable. Students learning the subject will struggle with this book, will find it daunting in places and will need to turn to other works. The need for a proper textbook of inhalation toxicology remains, I think, unmet. To anybody with a special interest in the compounds discussed at length, including CW agents, it will be indispensable: I am very glad to have a copy!

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