CORRESPONDENCE

A cohort mortality study and a case-control study of workers potentially exposed to styrene in the reinforced plastics and composites industry

Sir,—We have read with much interest the paper by Wong (1990;47:753–62) on workers exposed to styrene. The study is large and detailed methods for exposure assessment were applied. No statistically significant increases in cancer risk were detected overall although increases were seen in subgroups of the population, laryngeal cancer among men and leukaemias among highly exposed workers, for example.

The small number of deaths observed in this study is worth noticing. Of 15 908 workers enrolled, only 88 deaths were observed from all neoplasms. As a crude measure of comparison, the average number of deaths from neoplasms in four international occupational cohorts available in IARC is 2037 of 66 797 workers enrolled.[1–4] Reasons for the small number of cancer deaths are the young age of the cohort (half the workers entered the cohort before age 25), the short follow up (average time 7·7 years), and the incompleteness of the determination of vital status. Any of these reasons should caution against a premature negative evaluation of cancer risk in the reinforced plastics industry. The high rate of loss to follow up (16%), makes interpretation of results from this study especially problematic.

An increased risk was observed for respiratory cancers, which was shown to be unrelated to the degree of styrene exposure, or to exposure to acetone. Exposure to manmade mineral fibres (MMMF) could be another exposure worth considering, although we are unaware of any measurements of concentrations of respirable MMMF or of their physical characteristics in the reinforced plastics industry. If exposure data exist it would be interesting to evaluate any association with pattern of risk of lung cancer.

Admittedly, studies in the reinforced plastics industry pose many methodological problems because of the high mobility of workers (in the study presented by Wong, 46% of workers were employed for less than two years in the reinforced plastics industry), their frequently young age, and the small size of most factories. This study, as previous ones, does not seem to be yet able to exclude the presence of an increased cancer risk in this industry. The extension of the study in the future will provide more definitive results.

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1 Final Report of the International Agency for Research on Cancer (IARC). *Historical cohort study on man-made mineral fibre (MMMF). Production workers in seven European countries. Extension of the follow-up until 1982.* Lyon: International Agency for Research on Cancer, 1985.
2 International Agency for Research on Cancer. *Mortality and cancer incidence follow-up of an historical cohort of European welders.* Lyon: IARC, 1989. (IARC internal report No 89/003.)
3 International Agency for Research on Cancer. *Mortality and cancer incidence results of the European multi-centric cohort study of workers employed in the vinyl chloride industry.* Lyon: IARC, 1989. (IARC internal report No 89/007.)
4 Saracci R. Cancer mortality in an international cohort of workers exposed to chlorophenoxy herbicides and chlorophenols, 1991 (unpublished).

Author's reply:

Kogevinas and Boffetta discuss some of the limitations of my study of styrene workers. I agree with most of their comments; similar comments were made in the original paper.[1]

As pointed out there, the number of deaths was small for a number of causes, thus limiting the interpretation of the mortality patterns for these causes. A proper way to resolve this issue is to analyse the statistical power of the study for these causes of death, which was done. For example, the study had adequate power (80% power at the $p = 0.05$ level) to detect risks as small as 2·3 for lymphopoietic cancer and 3·4 for leukaemia. Thus although the small number of deaths was a limitation, the study did rule out risks higher than the ones estimated in this power analysis for certain causes of death.

With regard to the issue of an increased risk of laryngeal cancer, I believe that one should examine the data carefully and look beyond statistical significance in isolated findings. As pointed out by Bradford Hill in 1965, the interpretation of causation based on epidemiological data should follow a set of well structured criteria.[2] One of the major criteria is the consideration of dose-response relations.[3] Although quantitative exposure data were not available in the styrene study, duration of exposure and qualitative exposure information were. The excc of laryngeal cancer came only from short term workers who were employed in the industry for less than one year; no laryngeal cancer was seen among those who were employed for two years or longer. This observation argues against a causal interpretation. On the other hand, those with a high time weighted average of exposure had a higher risk of laryngeal cancer. Thus the cohort study offered conflicting data on laryngeal cancer.

Also, the finding of an increased risk of lung cancer among those exposed to the "hot" styrene process was puzzling. Since the risks of laryngeal and lung cancer are strongly influenced by cigarette smoking, a subsequent case-control study of respiratory cancer (larynx and lung) was conducted. In the case-control study, information on smoking was collected. The increase of respiratory cancer in various groups in the study could be explained by cigarette smoking. After adjusting for smoking, no increase was found with exposure to styrene.

This finding confirms the general impression that short term workers in general may have a very different lifestyle and, therefore, are exposed to confounding risk factors. In this styrene study the short term workers appeared to smoke more and were thus at an increased risk of laryngeal cancer.

The relatively high proportion of cohort members with unknown vital status was certainly a limitation. Because of death benefits from the social security system in the United States, it would be unlikely, however, for the families of these "lost to follow up" cohort members not to report any deaths to the Social Security Administration. Hence, there is no reason to believe that a higher proportion of cohort members with unknown vital status actually had died when compared with the rest of the cohort with known vital status.

Kogevinas and Boffetta raised the possibility of exposure to manmade mineral fibers (MMMF) in the study. I am not aware of any significant exposure to MMMF in this particular cohort.

Furthermore, based on some of the existing cohort studies on MMMF, only a modest increase in respiratory cancer was found among workers exposed to MMMF, and the interpretation of the relation between respiratory cancer and MMMF based on these cohort studies was problematic on several counts. The problems included higher risks among short term workers, lack of a dose-response relation, no control for cigarette smoking, and confounding exposures to asbestos and arsenic contamination.[4-7] Similar to the styrene study,[1] a more conclusive statement on MMMF and respiratory cancer can only be made through case-control studies with detailed information on confounding exposures.

I certainly agree that the study should be extended and such an updated study will have more adequate power. I believe, however, that the current cohort study of workers exposed to styrene, supplemented by the case-control study, offers valuable data on the mortality patterns of styrene workers. The results from this study should be interpreted in conjunction with other studies on workers exposed to styrene. As many of these studies are similarly limited in statistical power, data from these studies should be pooled together to maximise the information. Appropriate statistical methods for such a meta-analysis are available.[8] Perhaps the International Agency for Research on Cancer should take on this important task.

1 Wong O. A cohort mortality study and a case-control study of workers potentially exposed to styrene in the reinforced plastics and composite industry. *Br J Ind Med* 1990;47: 753–62.
2 Hill AB. The environment and disease: association or causation? *Proceedings of the Royal Society of Medicine* 1965; 58:295–300.
3 Wong O. Using epidemiology to determine causation in disease. *Natural Resources and Environment* 1988;3: 20–2.
4 Simonato L, Fletcher AC, Cherrie JW, *et al*. The International Agency for Research on Cancer study of MMMF production workers in seven European countries: extension of the follow-up. *Ann Occup Hyg* 1987;31:603–23.
5 Marsh GM, Enterline PE, Stone RA, Henderson VL. Mortality among a cohort of US man-made mineral fiber workers: 1985 follow-up. *J Occup Med* 1990;32:594–604.
6 Enterline PE. Role of manmade mineral fibres in the causation of cancer. *Br J Ind Med* 1990;47:145–6.
7 Rossiter CE, Douglas D. Role of man-made mineral fibres in the causation of cancer. *Br J Ind Med* 1990;47: 646–7.
8 Wong O, Raabe GK. Critical review of cancer epidemiology in petroleum industry employees, with a meta-analysis by cancer site. *Am J Ind Med* 1989;15:283–310.

NOTICE

CAES' 92: First announcement and call for papers

International conference on computer aided ergonomics and safety, Arctia Hotel Rosendahl, Tampere, Finland, 18–20 May 1992

The Conference is organised by Tampere University of Technology, Tampere, Finland and sponsored by the International Ergonomics Association, Finnish Ergonomics Society, Institute of Occupational Health, Finland, The Finnish Academy of Sciences, Technical Research Centre of Finland, and the Finnish Work Environment Fund.

The objective of this Conference is to provide an international forum to exchange information about recent advances in computer aided methods, techniques and tools for ergonomics, work safety, and health applications. Main areas of interest include: anthropometry and models of man, graphical tools for workplace design, assessment of static and dynamic workload, work measurement and labour standards, postural analysis and recording, biomechanical and physiological models, physical and mental rehabilitation, human cognitive modelling, CAD and ergonomic design process, CAD and participation in planning, safety and health information systems, intelligent data banks and expert systems, neural nets applications in safety and health, safety and risk analysis, accident investigation and prevention, process incident control, and modelling of work environment exposure.

Books and computer software will be exhibited.

Proposals for participation may include technical papers, workshops, software demonstrations, and other presentations.

Submission deadlines are: receipt of abstracts 30 October 1991; notification of the review outcome 30 November 1991; submission of papers 15 January 1992.

All abstracts should be sent to: Professor Markku Mattila, Conference Chairman, Department of Mechanical Engineering, Tampere University of Technology, Box 527, SF-33101 Tampere, Finland, Tel +358-31-162621. Fax +358-31-162671.

The Conference Proceedings will be published as an edited book.

International Programme Advisory Board Chairman: Professor W Karwowski, USA.

Author's reply

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Notes