

Recent epidemiologic studies of occupational cancer in Finland

by Sven Hernberg, MD¹

Occupational cancer has been one of the main areas of epidemiologic research at the Finnish Institute of Occupational Health for many years. Although the populations exposed to any specific carcinogen tend to be small in a country with a population of 4.9 million only, other circumstances render research in cancer epidemiology fruitful. First and foremost the country's registers are good, especially the Finnish Cancer Register, which was established already in 1952 (12) and whose coverage is virtually 100 %. Most of the cancer studies have been conducted in close collaboration with the Cancer Register. In addition the population registers are good. Thanks to their high quality, usually more than 98 % of a cohort can be traced. Furthermore, close collaboration with skilled occupational hygienists has greatly improved the quality of the exposure data used in the epidemiologic studies. These circumstances tend, at least partly, to compensate for the small size of the study populations.

In 1980, at the first US-Finnish joint symposium held in Cincinnati, Tola reviewed the Finnish occupational cancer studies that had been conducted up to then (13). The present overview highlights the investigations that have been published thereafter.

Silica

Both patients with manifest silicosis and workers exposed to silica dust in quarry work have been studied. A mortality investigation was conducted among 961 patients with silicosis diagnosed between 1935 and 1977 and recorded in the Finnish Register of Occupational Diseases (8). There was a consistent finding of excess lung cancer deaths both in the cohort as a whole [observed 80, standardized mortality ratio (SMR) 312, 99 % confidence interval (CI) 230–414] and in all sub-cohorts formed of silicosis patients according to the type of industry in which silicosis was acquired, ie, mining, stone industry, steel and iron foundries, and "others." Confounding by smoking seemed an unlikely explanation for all the excess lung cancer, and other carcinogenic exposures, such as radon daughters in mines and polycyclic aromatic hydrocarbons in foundries, may have been responsible for at least part of it.

Pure quartz exposure occurs in quarries, however. In a still ongoing project, granite workers have been followed since 1971 (6, 7). The study group is formed of 1 026 workers, hired between 1940 and 1971 by

quarries situated in three counties in Finland. By the end of 1985, 59 tumors had been observed, while 54.4 were expected. Of the tumors, 31 were lung cancers (expected 19.9) and 18 were gastrointestinal cancers (expected 11.6). The mortality for lung cancer became more pronounced when allowance was made for a latency period of 15 years or more (28 observed, SMR 220, $P < 0.001$). Smoking habits were surveyed in a questionnaire sent to living workers and to the relatives of deceased workers; they did not deviate essentially from those of Finnish industrial male workers in general. Only three of the lung cancer patients had silicosis. The results were interpreted as indicating that quartz exposure per se may be an etiologic factor in the initiation or promotion of malignant neoplasms.

A joint Nordic register study has also investigated the connection between silica exposure and lung cancer (9). This study showed an excess lung cancer risk for foundry workers in all the Nordic countries and for miners in Sweden. Stonecutters showed a significant excess lung cancer risk in both Finland and Denmark. Excess lung cancer risks furthermore occurred for Finnish miners, Finnish men in excavation work, and Danish glassworkers.

Paper and pulp production

There have been some suggestions that work in pulp and paper production may be connected with excess cancer risk, but the literature is far from conclusive. A recent study of Finnish pulp and paper workers found a rather convincing indication of excess lung cancer risk (4). The study comprised 3 545 workers in a large Finnish pulp and paper mill. The cohort included workers with continuous employment of at least one year between 1945 and 1961, and it was followed until the end of 1980. The overall cancer incidence was not increased, but there were 78 lung cancer cases observed among the men while 62.6 were expected [standardized incidence ratio (SIR) 125, 95 % CI 98–155]. The excess was the most prominent for male board mill workers (40 observed, 18.1 expected, SIR 222, 95 % CI 158–302), especially when allowance was made for 20 years' latency (25 observed, 7.8 expected, SIR 323, 95 % CI 209–476). In addition papermill workers showed a slightly elevated lung cancer risk (SIR 197, 95 % CI 102–345), while no such risk was evident for sulfite mill, sulfate mill, or maintenance workers. The number of female workers was too small to allow any conclusions with respect to them. Smoking habits were

¹ Institute of Occupational Health, Helsinki, Finland.

inquired into by means of a questionnaire sent to a randomized sample of the cohort. The pulp and paper workers had smoked less than men in general in 1956, and equally much in 1981, except for the sulfate mill subcohort, which had smoked more. Hence the excess cancer risk found in the board mill and the paper mill cannot be explained by confounding by smoking. The causative agent could not be identified with certainty, although asbestos, which may have occurred as an impurity of talc, is high on the list of suspects. Other potential carcinogens, such as auramine and chlorinated phenols, have also earlier been used in board production.

Wood industry

A nested case-referent study on respiratory cancer has been carried out among male workers employed in the particleboard, plywood, sawmill, and formaldehyde glue industries (5). The initial objective was to study the effects of formaldehyde exposure, but the detailed exposure data available also made it possible to consider a number of other chemical exposures, such as pesticides, phenol, and terpenes. From within the cohort of 3 805 men, 57 patients with verified respiratory cancer (codes 160—162.1, 141, and 143—148 of the seventh revision of the International Classification of Diseases) were defined as cases, and 171 men without respiratory cancer from within the cohort were matched for birth and used as referents. The comparison of exposures was carried out according to work histories and job exposure matrices for each plant. Significantly (one-sided test, 5 % level) increased odds ratios were found for exposure to pesticides and phenol. For phenol, the increased odds ratio was partly explained by smoking and exposure to pesticides. Exposure to terpenes and other heating products of coniferous wood was associated with respiratory cancer when the duration of exposure exceeded five years.

No odds ratio was significantly increased for formaldehyde exposure (10). A later expansion of the study to 7 307 men with a few more years of follow-up yielded 136 cases of respiratory cancer (unpublished). By similar methodology, an odds ratio of 2.24 ($P < 0.05$, one-sided) was found for pesticide exposure when a minimum latency of 10 years was allowed for. When adjusted for survival status and smoking, the odds ratio fell to 1.71 [not significant (NS)]. For phenol exposure the odds ratio was 2.16 (NS), allowing for 10 years of latency, and 1.71 (NS) when adjusted for survival status and smoking. For formaldehyde exposure of at least 3 ppm-months, the corresponding odds ratios were close to unity.

Shipyards and machine shops

A large cohort study investigated the cancer incidence of 12 693 shipyard and machine-shop male workers (14). Of them, 1 689 were welders, 4 308 platers, 6 003

machinists, and 693 pipe fitters, all of whom had been employed for at least one year during 1945—1960. All the welders had welded only mild steel. The number of person-years was 304 682. The cancer incidence was ascertained from the Finnish Cancer Register. Smoking habits, as obtained in a questionnaire sent to a sample of 961 workers, were similar in the different categories and did not differ from those of the general male population, from which the expected values were computed. The total number of cancers was 611 (expected 629) among the shipyard workers and 376 (expected 388) among the machine-shop workers. The lung cancer incidence was increased among the shipyard workers (observed 227, expected 192). This excess occurred in all worker categories and was the most marked for the pipe fitters and platers. The incidence of laryngeal cancer was slightly elevated among the machine-shop workers (observed 39, expected 31) but not among the shipyard workers. No marked excess could be found for other types of cancer, not even for mesothelioma. The results indicated that the excess risk for welders was only marginal and, since these welders had been heavily exposed to welding fumes in the past, that the risk for today's welders is probably low.

Phenoxy acids

In 1972, a prospective cohort of phenoxy acid herbicide applicators was started (11). The study is still in progress and will be updated this year. The cohort comprises 1 971 male workers who had sprayed herbicides for at least two weeks during 1955—1971. By the end of 1981, 26 cancer cases had occurred, while 36.5 were expected. None of the cases was soft tissue sarcoma or lymphoma; only one was a multiple myeloma (expected 0.2). The short follow-up time, the small size of the study (16 694 person-years), and the liberal criteria for minimum exposure render the results inconclusive. Some of these weaknesses will improve with time, however.

Primary liver cancer

The first Finnish case-referent study on primary liver cancer and occupational exposures was based on questionnaires sent to the relatives of deceased patients with liver cancer diagnosed in 1979 and 1980 and to the relatives of deceased coronary infarction patients (reference group) (1). The exposure histories of a total of 126 cases and 175 referents could be obtained.

The occupational histories were coded blindly by an industrial hygienist, and the correctness of the cancer diagnoses was ascertained by a pathologist. The results showed no remarkable difference for the men, but six women with liver cancer had been exposed to organic solvents as compared to none of the referents. This result, which was considered as suggestive only, prompted a new, similar study on cases of primary liver cancer diagnosed in 1976, 1977, 1978, and 1981 (2).

Again, patients who had died of coronary infarction were used as referents. In addition another disease category, stomach cancer, was examined to test the possibility that infarction patients, for some reason, would have introduced bias. After losses due to failure to find any relative, and to nonresponse, occupational histories of 375 liver cancer cases, 478 stomach cancer referents, and 385 coronary infarction referents were available for the analysis. The results showed no increased risk of liver cancer for men exposed to solvents. All the odds ratios were well below 1. Among the women with liver cancer, seven had been exposed to solvents, while only three stomach cancer referents and two coronary infarction referents had had solvent exposure. When the women with liver cancer were compared with the female stomach cancer referents, the female infarction referents, and both groups of referents combined, the odds ratios were 2.6 (90 % CI 0.9–7.9), 3.2 (90 % CI 0.9–11.3), and 2.88 (90 % CI 1.2–7.4), respectively. Past alcohol use also increased the risk for liver cancer, especially among the men, but also to some extent among the women. However, when adjustment was made for alcohol use, it appeared that the confounding effect was *negative*, especially so for the women, among whom none of the exposed cases had used alcohol more than occasionally. In fact, the odds ratios were 8.6 and 6.4, respectively, when the comparison was restricted to those with no or occasional alcohol use. Combining the results of both studies yielded an odds ratio of 7 (95 % CI 2.0–26.3) for the women. Closer scrutiny revealed that altogether nine women with cancer but only two of the referents had been exposed to chlorinated hydrocarbons in addition to other solvents. Such exposure was far less common among the men irrespective of whether they were cases or referents. This observation strongly indicates chlorinated hydrocarbons (trichloroethylene, perchloroethylene, and carbon tetrachloride alone or in combination) as the cause of the increased cancer risk among the women. It also explains the seeming sex difference, because exposure to chlorinated hydrocarbons is far more common in “female jobs.” The exposed men had mostly been painters.

Current studies

In addition to the already mentioned studies, some others are in the data-analysis stage. They include a mortality study of miners [which not only suggests an increased risk of lung cancer, but also of coronary heart disease (Ahlmán et al, in preparation)], a large case-referent study on renal cancer and occupational exposures (Partanen et al, in preparation), and a case-referent study on mesothelioma and exposure not only to asbestos, but also to other fibers. It can finally be mentioned that the Institute of Occupational Health maintains a Register of Employees Occupationally Ex-

posed to Substances and Working Processes Possibly Causing Cancer Risk (ASA), which was established in 1979 in accordance with Convention No 147 of the International Labour Organisation. This register is based on employers' reports of all departments in which carcinogenic agents are used, and it lists all workers with (i) definite, (ii) probable, and (iii) possible exposure to carcinogens (3). Because the exposure data are rather crude, it remains to be seen if this register will be of any use in future research.

References

1. Hernberg S, Korkala M-L, Asikainen U, Riala R. Primary liver cancer and exposure to solvents. *Int Arch Occup Environ Health* 54 (1984) 147–153.
2. Hernberg S, Kauppinen T, Riala R, Korkala M-L, Asikainen U. Increased risk for primary liver cancer in women exposed to organic solvents. *Scand J Work Environ Health* (in press).
3. Herva A, Partanen T. Computerizing occupational carcinogenic data in Finland. *Am Ind Hyg Assoc J* 42 (1981) 529–533.
4. Jäppinen P, Hakulinen T, Pukkala E, Tola S, Kurppa K. Cancer incidence of workers in the Finnish pulp and paper industry. *Scand J Work Environ Health* 13 (1987) 197–202.
5. Kauppinen TP, Partanen TJ, Nurminen MM, Nickels JI, Hernberg SG, Hakulinen TR, Pukkala EI, Savonen ET. Respiratory cancers and chemical exposure in the wood industry: A nested case-control study. *Br J Ind Med* 43 (1986) 84–90.
6. Koskela R-S, Klockars M, Järvinen E, Kolari PJ, Rossi A. Cancer mortality of granite workers. *Scand J Work Environ Health* 13 (1987) 26–31.
7. Koskela R-S, Klockars M, Järvinen E, Rossi A, Kolari PJ. Cancer mortality of granite workers 1940–1985. International Agency for Research on Cancer, Lyon (in press).
8. Kurppa K, Gudbergsson H, Hannunkari I, Koskinen H, Hernberg S, Koskela R-S, Ahlman K. Lung cancer among silicotics in Finland. In: Goldsmith DF, Winn DM, Shy CM, ed. *Silica, silicosis, and cancer*. Praeger Special Studies, Praeger Scientific, New York, NY 1986, pp 311–319.
9. Lynge E, Kurppa K, Kristofersen L, Malker H, Sauli H. Silica dust and lung cancer: Results from the Nordic occupational mortality and cancer incidence registers. *J Natl Cancer Inst* 77 (1986) 883–889.
10. Partanen T, Kauppinen T, Nurminen M, Nickels J, Hernberg S, Hakulinen T, Pukkala E, Savonen E. Formaldehyde exposure and respiratory and related cancers: A case-referent study among Finnish woodworkers. *Scand J Work Environ Health* 11 (1985) 409–415.
11. Riihimäki V, Asp S, Pukkala E, Hernberg S. Mortality and cancer morbidity among chlorinated phenoxyacid applicators in Finland. *Chemosphere* 12 (1983) 779–784.
12. Saxén E, Teppo L. Finnish Cancer Registry 1952–1977: Twenty-five years of a nationwide cancer registry. The Institute for Statistical and Epidemiological Cancer Research, Helsinki 1978.
13. Tola S. Overview of Finnish epidemiologic studies on occupational cancer. *Scand J Work Environ Health* 7 (1981): suppl 4, 133–139.
14. Tola S, Kalliomäki P-L, Pukkala E, Asp S, Korkala M-L. Cancer incidence among welders, platers, machinists and pipe fitters in shipyards and machine shops. *Br J Ind Med* 45 (1988) 209–218.