Incidence of cancer among ferrochromium and ferrosilicon workers

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ABSTRACT   The results are presented of a study of the overall mortality and the incidence of cancer in male workers producing ferrosilicon and ferrochromium. Although the study included all present and retired workers employed in the factory for more than one year from 1928 until 1977 inclusive, the incidence of cancer in those 976 workers who started work before 1 January 1960 was studied in particular. Both the overall mortality and the incidence of cancer for all sites were lower than expected when compared with the national expected figures. Nine cases of lung cancer were found in the total population—seven in the ferrochromium subpopulation against expected rates of 3·1 and 1·8 when using national and local expected rates respectively as reference, and less than one expected case when using an internal reference population. A 1·5 O/E ratio was found for prostatic cancer in the whole study population. The results indicate that the increased incidence of lung cancer in the ferrochromium group has a causal relationship to occupational exposure. Perforation of the nasal septum was found in two present ferrochromium workers, and hexavalent chromium was found in the working atmosphere at the ferrochromium arc-furnaces during an industrial hygiene survey carried out in 1975. It is therefore concluded that the raised incidence of lung cancer is partly due to exposure to chromates. The results do not support the suggestion that exposure to chromic compounds entails a cancer hazard similar to that of exposure to hexavalent chromium compounds.

Firm epidemiological evidence has been presented showing an association between prolonged inhalation of hexavalent chromium compounds and the development of cancer of the respiratory tract in exposed workers.[1] Such association has been shown both in workers exposed to dichromates[2 3] and in workers exposed to chromium pigments.[4 5] Increased incidence of cancer in the gastrointestinal tract has also been suggested in chromate workers by Taylor[6] and Langård and Norseth (at the XIX International Congress on Occupational Health, Dubrovnik, 25-30 September 1978 (unpublished observations)).

Mancuso (at the International Conference on Heavy Metals in the Environment, Toronto, 27-31 October 1975 (unpublished observations)) and Pokrovskaja and Shabynina[7] have suggested that there is also an association between prolonged human exposure to trivalent chromium compounds

and development of cancer in the respiratory tract. So far these studies have not been confirmed by other epidemiological studies. From a theoretical point of view, however, the suggested carcinogenic effect of trivalent chromium is of great interest because chromium is bound to nucleic acids only in the trivalent state.[8-10]

The present study was carried out to discover if workers exposed to trivalent chromium compounds do, in fact, have an increased risk of developing lung cancer or cancer at other sites. The study was performed in parallel with a study by Axelsson et al.[11] Though the sources of information were different, the two studies have been carried out in as similar a fashion as possible.

The study plant is located in an isolated community at one of the Norwegian fjords and started production in 1928. The work force has been stable, and several workers were employed continuously from 1928 until 1977 inclusive.

The major products manufactured in the plant have been ferrosilicon and ferrochromium, and

production was started in 1928 and 1932 respectively. The processing of these products is based on the electrothermal reduction of quartz and chromite ore with coke. Currently there are four ferrosilicon furnaces that are all open three-phase units. The ferrochromium alloys are batch-produced in eight open three-phase arc-furnaces. During the 50 years of production there have been several changes in the production routines, indicating changes in levels of dust and fume exposure. No data were available on dust composition in previous years.

Until 1965-6 the major portion of the quartz needed for the ferrosilicon production was mined from open quarries owned by the company, and until 10 years ago the plant produced its own electrode material. Some asbestos has been used for heat protection and insulation in different departments of the factory. According to information provided by the company, there has been no difference in the use of asbestos between the ferrosilicon furnaces and the ferrochromium furnaces.

The number of employees increased gradually from 50 in 1928 to about 250 in 1932 and about 450 in 1940. From 1940 to 1977 the number has varied from 450 to 550. The total number of workers during the study period has been about 2800, including those with a few months' employment.

Methods

The epidemiological method adopted in this study has been described earlier by Langård and Norseth[5] and Pedersen *et al.*[12] The main principle of the method is to identify all individuals who meet the criteria for membership of the study population and to compare this population with a constructed

Norwegian population. It was possible to ascertain the incidence of cancer in the reference population from registrations in the Cancer Registry of Norway.[13 14] The cancer registry contains the cancer incidence rates for all cancers and their localisation and is presumably complete for all cancers diagnosed in the country from 1953 to date. Computation of expected deaths was based on the age-specific national mortality rates, by five-year age groups, for each calendar year during 1953-76.

A list containing the names of all employees with employment time exceeding six months was compiled from a personnel register provided by the company and information obtained from the employees' health record, which dated back to 1946. This list contained 1761 names. The completeness of the list was checked and confirmed through individual interviews with 10 different workers, some of whom had been employed in the plant since the start of production and who had lived in this community all their lives. Based on this information, the study population was defined as men with employment time exceeding one year who had started working at the plant before 1 January 1960. Those who died before 1 January 1953 (25) were excluded, as were those with an unidentified date of birth (nine) and one person whose year of starting employment was unknown. These limitations on the study population reduced the number of subjects to 976. Since the criteria for participation included a minimum period of employment, the calculation of expected mortality and incidence of cancer began at the conclusion of the minimum employment period.

By a combination of information from three different sources, a continuous job characterisation could be given for 968 of the members of the study

Table 1 *Observed (O) and expected (E) cases of cancer (all sites, stomach cancer (ICD 151), lung and bronchial cancer (ICD 162/163), and cancer of the prostate (ICD 177)) in the study population. All new cases of cancer from January 1953 until 1977 inclusive are included (ICD codes 140-204 except skin cancer (191))*

	No of workers	All deaths*		All cancers		151		162/163		177		Person years 1953-77
		O	E	O	E	O	E	O	E	O	E	
Various jobs	80	16	18·16	5	5·69	0	0·82	1	0·67	1	0·91	1837
Ferrosilicon	243	53	67·51	15	23·90	3	3·57	0	2·78	3	4·24	5710·5
Ferrochromium	325	52	63·12	23	23·49	5	3·18	7†	3·10	5	3·27	7603·0
Internal maintenance	88	12	14·92	3	4·77	0	0·65	0	0·57	2	0·65	2035·0
Quartz quarry	45	8	11·59	3	4·00	0	0·60	0	0·43	2	0·72	1062·0
Office workers	41	3	7·92	2	2·81	0	0·40	0	0·33	1	0·43	946·5
Electric shops	49	7	12·55	6	4·60	0	0·71	0	0·45	3	0·92	1138·5
External maintenance	39	10	11·80	2	4·23	0	0·67	0	0·41	2	0·86	901·0
Internal transport	63	21	20·90	5	5·61	2	0·86	1	0·68	1	0·96	1471·5
Electrode factory	3	0	0·73	0	0·34	0	0·05	0	0·03	0	0·07	72·0
Total	976	182	228·20	64	79·44	10	11·51	9	9·45	20‡	13·03	22777·0

*Crude death rate for period 1953 until 1976 inclusive.
†p = 0·08, one-tailed.
‡p = 0·06, one-tailed.

population. These sources of information were as follows. (1) The personnel list provided by the company, which included job descriptions of about 40% of the workers. (2) Detailed information on previous and current occupational history that had been written on the health records of each worker who had been employed during the period 1946-52. Since very few of the study population appeared to have stopped working before 1946 this source of information was of great help for the job characterisation. (3) Job descriptions based on the previous two sources of information that were supplied and corrected through interviews with those 10 workers mentioned above. Ten different occupational categories were defined (table 1). The eight workers with unsatisfactory job descriptions were included under the category "various jobs." All job classifications were carried out before identification of the cancers and the causes of death.

The occupational category in which each worker spent the greatest amount of time during his employment at the plant was used to determine to which subpopulation he should belong. Membership of the subpopulation was also determined before identification of the cancers and the causes of death.

All members of the study population were considered "under observation" from the beginning of 1953 until 1977 inclusive or, in the case of later first employment, from one year after the appointment in the plant.

A complete industrial hygiene survey was carried out during 1975. In this investigation the total concentration of dust at different workplaces in the plant was measured by means of full-shift sampling with both personal and stationary air samplers. The dust samples were collected on 37 mm, 0·8 μm Millipore cellulose ester membranes using Casella personal samplers and Edwards stationary air samplers. The total concentration of dust was determined gravimetrically. Subsequently the membranes were dissolved in acid, and the total amount of chromium was determined by atomic absorption spectroscopy.[15]

Hexavalent chromium compounds are considered to be potent carcinogens while it is doubtful whether chromic compounds are carcinogenic.[10] Therefore it was important to differentiate between these groups of compounds when monitoring the working atmosphere. Abell and Carlberg[16] have indicated that reduction of chromium from the hexavalent to the trivalent state may take place on cellulose ester membranes during storage.

To discriminate between these two valency states a separate study was carried out. Assuming that most of the water-soluble chromium is in the hexavalent state, personal dust samples of workers employed at the furnaces were collected on 37 mm, 2 μm Millipore PVC membranes where hexavalent chromium would remain unchanged for some time.[16] Immediately after the sampling procedure was finished, the membranes were extracted with 100 ml distilled water and analysed for chromium by atomic absorption spectrometry.[15] The membranes, including the remaining dust, were subsequently dissolved in acid and analysed for chromium by the same procedure.

The expected and observed numbers were used to calculate the risk ratios. It was assumed that the observed numbers of cases followed Poisson distributions with the expected numbers as the modes, and Poisson distributions were used for significance testing.

Results

Table 1 shows overall mortality data and incidence of cancer in the study population and in the subpopulation, restricted to those individuals who started employment before 1960. This table also gives the age-adjusted incidence of three particular cancer sites and their distribution between the subpopulations. The numbers of person years given in table 1 and table 5 cover the period 1953-77 and therefore apply to the calculation of expected cases of cancer and not to the calculation of expected deaths, which is based on the period 1953-76.

The mortality data and the data on the incidence of all cancers show that the figures for "observed" are lower than "expected" in both cases. A slight excess of stomach cancer was found in the ferrochromium subpopulation. When considering occurrence of cancer in the respiratory tract, which was the main subject of the present study, the table shows that seven cases were found in the ferrochromium subpopulation against 3·1 expected (O/E = 2·26; $\chi^2(1)$ = 2·06; p = 0·08, one-tailed).

The total Norwegian male population was used as reference for the incidence of cancer. This includes the assumption that the incidence of cancer in the county of Hordaland, where the plant is located, is identical with that of the total male population. It is known from the data presented by the Cancer Registry of Norway[17] that the age-corrected incidence of lung cancer in the rural western region of the country is 58% of the incidence in the whole country. This means that using the total male population as reference implies an overestimation of the risk of lung cancer for each individual of the study population. (O/E modified by 0·58 = 3·89; $\chi^2(1)$ = 2·45; p = 0·06, one-tailed.)

Table 2 *Occurrence of lung cancer*

	Observed	Expected	O/E
Ferrochromium workers	7	3·10	2·66
Internal referents*	2	6·35	0·31

*All workers except ferrochromium workers.

Furthermore, when using the whole non-ferrochromium population included in the study as an internal reference, the O/E ratio for lung cancer in the ferrochromium group becomes 8·5 as calculated from the figures in table 2 (2·66/0·31 = 8·5; $\chi^2(1)$ = 3·76; p = 0·026, one-tailed). Since the ferrosilicon group has carried out similar work at the ferrosilicon furnaces, this group might be considered as a valid internal reference population for the ferrochromium group. To some extent both these subpopulations have been exposed to asbestos in their work and possibly also to low atmospheric levels of polycyclic aromatic hydrocarbons. Based on information provided by the company on the previous use of asbestos in the plant, there is no reason to believe that the exposure to this known carcinogen has been significantly different in these two subgroups. As shown in table 1, no cases of lung cancer were observed in the ferrosilicon group.

Nine cases of lung cancer were identified in the whole population (table 1). To locate further possible specific carcinogenic agents in the working atmosphere, the detailed employment history of the nine workers with lung cancer is presented in table 3. As can be calculated from this table, 58% of the employment time of these was associated with the ferrochromium production. Although the comparable figures cannot be exactly calculated for the rest of the population, these figures present further evidence that there is an association between the

development of lung cancer and work at the ferrochromium furnaces. Only one case of lung cancer was diagnosed before 1969 and six of the seven cases in the ferrochromium group were diagnosed after 1971.

The results from the gravimetric dust measurements and the chromium analyses are presented in table 4, showing that the total dust concentrations in these two departments were similar. With few exceptions, the total chromium content of the dust was below the current TLV (1 mg/m³) for trivalent chromium compounds. The content of water-soluble chromium ranged from 11% to 33% of the total chromium. Consequently, the current TLV for chromates (0·1 mg/m³) was exceeded in some instances.

In a medical survey carried out during 1976 on 60 of the ferrochromium workers, who had been employed for 15 years or more, and on 105 workers with different exposure, two septal perforations were found in the ferrochromium group and none in the other group. These two workers had been exposed to chromium-containing atmosphere from the 1930s onwards, which indicates that hexavalent chromium was present in the working atmosphere in the early years of ferrochromium production. Exposure to hexavalent chromium elsewhere could be excluded.

As shown in table 1, a significant excess of cancer of the prostate is shown in the whole study population and a slight, non-significant excess in the ferrochromium subpopulation. There is also a slight excess of prostatic cancer in the electric shop workers and in the maintenance group, neither of which is statistically significant.

There is a long time-lag ("latent period") between the start of a tumour and its clinical manifestation.[18] This problem has been considered in this study. In

Table 3 *Distribution of work labels among workers in whom lung cancer had been diagnosed. Figures give duration of exposure under different categories in years*

Age when cancer was diagnosed	Time of first employment	Year of diagnosis	Work label*									
			1	2	3	4	5	6	7	8	9	10
63	1950	1964	10									
75	1928	1969		5	28							
70	1928	1971	4								31	
65	1950	1971			10							
54	1946	1972			26							
65	1947	1974			5							
55	1934	1975			17					10	15	
72	1949	1976			12							
79	1949	1976	4		10							
Total			18	5	108					10	46	

*Work labels: 1 = various jobs, 2 = ferrosilicon, 3 = ferrochromium, 4 = internal maintenance, 5 = quartz quarry, 6 = office workers, 7 = electric shops, 8 = external maintenance, 9 = internal transport, and 10 = electrode factory.

Table 4 *Atmospheric total dust and chromium measurements in 1975*

Work operation	No of samples	Mean dust conc mg/m³	Range	Mean chromium‡ conc mg/m³	Range
Ferrosilicon department					
Tapping*	10	5·7	3·1-10·3		
Charging*	9	11·9	6·1-26·4		
Electrode supply*	9	10·1	5·8-15·4		
Packing*	10	8·3	2·2-19·0		
Packing room†	11	3·0	1·2- 4·6		
Tapping floor†	6	2·9	0·8- 4·9		
Top electrode†	5	14·5	3·2-27·9		
Maintenance people					
General maintenance*	9	15·6	4·0-46·0	0·09	0·02-0·37
Transport men*	9	12·8	5·6-30·1	0·01	0·01-0·03
Ferrochromium department					
Potmen*	20	6·3	4·0-15·7	0·04	0·02-0·07
Cleaner balers*	5	18·2	10·5-23·9	0·09	0·05-0·13
Crane driver*	10	4·6	3·1- 7·6	0·04	0·01-0·05
Packing*	10	4·9	2·3- 8·3	0·29	0·05-1·30
Charge floor†	5	4·8	2·8- 8·4	0·05	0·03-0·07
Top electrode†	3	15·5	13·9-17·8	0·17	0·15-0·19
Packing†	18	1·9	0·3- 5·5	0·19	0·01-1·34

*Personal samples.
†Static samples.
‡11% to 33% of chromium was water soluble.

table 5 the relation between the date of starting employment at the plant and tumour incidence at some specific sites has been considered. Except for the subpopulation that started working between 1940 and 1949, where there is an excess of lung cancer compared with expected figures, there is no obvious relation between the time of first employment and cancer development.

Discussion

As shown in a recent publication from the Cancer Registry of Norway,[17] there is an obvious geographical variation in the incidence of cancer of the prostate. The incidence in rural areas in the western region of the country is slightly higher than in rural areas in the country as a whole. This difference, however, does not fully explain the increased O/E

ratio in the present study. Axelsson *et al*[11] also showed an excess of cancer of the prostate. In this respect the two studies present analogous results. The increased incidence of prostatic cancer, however, was associated with different subpopulations in the two studies. Therefore, the demonstrated excess of prostatic cancer is unlikely to be related to specific factors that are present in the working atmosphere in the study plants.

The present study has shown an increase in the incidence of lung cancer in a population that has been exposed for a long period to the smoke and dust derived from ferrochromium-producing arc-furnaces. The raised incidence is present both when comparing with an external and with an internal reference group. The observed accumulation of cases of lung cancer in the employees who started working between 1940 and 1950, combined with the

Table 5 *Observed (O) and expected (E) deaths (total number of cancer cases, stomach cancer (ICD 151), lung and bronchial cancer (ICD 162/163), and prostate cancer (ICD 177)) in relation to time of first employment in plant. All new cases from January 1953 until 1977 inclusive are included (ICD codes 140-204 except skin cancer (191))*

Years of first employment	No of workers	All deaths*		All cancers		151		162/163		177		Person years
		O	E	O	E	O	E	O	E	O	E	
1928-9	129	68	77·06	20	22·95	4	3·93	2	2·19	6	5·16	3062·0
1930-9	191	35	57·02	16	21·61	2	3·10	1	2·76	6	3·63	4566·5
1940-9	368	51	61·06	22	22·68	4	3 00	4	2·93	7	2·90	8806·5
1950-9	288	28	33·05	6	12·20	0	1·49	2	1·57	1	1·34	6342·0
Total	976	182	228·20	64	79·44	10	11·51	9	9·45	20	13·03	777·0

*Crude death rate for period 1953 until 1976 inclusive.

demonstrated accumulation of cases 25-30 years later, might indicate that exposure to the carcinogenic agents occurred during this period, but no obvious explanation can be found for this suggested relationship.

The results have been presented with only a few tests of statistical significance. There are different methodological reasons for this: the O/E ratio for lung cancer varies considerably depending on which reference group is being used—from 7/3·1 and 7/1·8 when using external control groups to 8·5/1 for an internal reference group. Since the internal reference group is recruited from the same local population as the ferrochromium group, this might be considered the most valid reference population. The fact that the internal reference group also has quite a similar occupational history to the ferrochromium group strengthens the validity of this group as a reference population. Therefore, it seems most relevant to consider the O/E ratio 8·5/1 as the relative risk for lung cancer in the ferrochromium group. That the relevance of the different reference populations is uncertain and the fact that the most relevant reference group, the ferrosilicon workers, cannot be used due to lack of observed cases, seems to make significance testing irrelevant.

The demonstration of hexavalent chromium in the working atmosphere around the ferrochromium furnaces and the presence of perforation of the nasal septum in two ferrochromium workers together make it likely that the ferrochromium workers have been exposed to significant amounts of hexavalent chromium throughout the whole production period. Chromate-induced perforations of the nasal septum are considered to occur only when the atmospheric chromate concentration exceeds 0·1 mg/m³.[19] Provided this assumption is correct, the ferrochromium workers must have been exposed to chromate concentrations exceeding 0·1 mg/m³ in the working atmosphere during previous years. Therefore, the estimate to be tested with a significance test involves a bias of unknown magnitude, which also makes significance testing quite irrelevant.[20]

Long-lasting human exposure to chromates at high atmospheric concentrations induced lung cancer at O/E ratios in the range of 20/1 to 40/1.[1 5 6] In the present investigation one can only guess at what level the exact atmospheric chromate concentration has been in previous years. Based on the observations which have been discussed, however, it seems reasonable to assume that the atmospheric chromate concentration has been high enough to contribute to the increased incidence of lung cancer in the ferrochromium group.

The finding of a risk ratio for cancer of the respiratory tract that is much lower than that found for chromate exposure in previous chromate studies does not support Mancuso's suggestion in Toronto in 1975 that chromic compounds are carcinogenic to the same extent as chromates. The lack in increase in the incidence of lung cancer found by Axelsson *et al*[11] supports the view that inhalation of chromic compounds is not a significant carcinogenic hazard.

No information was available on the smoking habits of the retired workers. Smoking habits among the processing workers in the plant were studied at the beginning of 1976. Between 55 and 60% were smokers at that time, with a slight variation between the different subpopulations. This is very similar to the figures reported by Zeiner-Henriksen[21] for the whole country. Therefore, smoking habits are not likely to be a major confounding factor in relation to the incidence of cancer in the present study.[22]

The reduced overall mortality and the reduced incidence of all cancers observed in this study is another finding that deserves a short comment. This phenomenon is also observed by others who have carried out epidemiological studies on large populations.[23] The present study shows that such an observation does not justify the conclusion that no health hazard is present in the working conditions. Even when the overall incidence of cancer is found to be considerably lower than the expected figures, small subgroups may still have been at significant risk of cancer. The present study shows that an increased risk may be easily hidden in a low overall incidence of cancer. The results therefore emphasise the necessity of an accurate working history for each individual when carrying out population studies such as the present one.

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[2] Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.

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