A cohort study of bronchial carcinomas in workers producing chromate pigments

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Langård, S. and Norseth, T. (1975). *British Journal of Industrial Medicine*, 32, 62-65. **A cohort study of bronchial carcinomas in workers producing chromate pigments.** A cohort study of the incidence of bronchial cancer in male workers in a small company producing chromate pigments is presented. Altogether 133 workers had been employed by the company from the time production was started in 1948 until the end of 1972. Workers with more than three years employment were included in the study, and three cases of bronchial carcinoma were found among the 24 workers who fulfilled this requirement. Based on the data of the Cancer Registry of Norway the risk of bronchial cancer for a corresponding group of the general population was found to be 0.079, which gives a risk ratio for exposed workers of approximately 38. The average age of the cancer patients was as low as 50 years at the time of diagnosis. All workers in the company had been exposed mainly to zinc chromate dust, and the exposure levels of the workers developing bronchial cancers had probably been from 0.5 to 1.5 mg Cr/m³ for six to nine years. Two of the three patients were smokers. It is assumed that exposure to chromate pigments, and probably to zinc chromate, may be related to the increased incidence of bronchial cancer in this group of workers. The possibility of a contributing effect of tobacco smoking in at least two of the three cases cannot be ruled out.

Although Newman (1890) described adenocarcinoma of the inferior turbinate of the nose in a worker producing chromate pigment, Kölsch, as reviewed by Lehman (1932), was the first to suggest a connection between exposure to chromate dust and lung cancer. He observed two cases of lung cancer among several hundred chromate workers in Ludwigshafen. Pfeil (1935) and Alwens and Jonas (1938) reported 25 cases of respiratory cancer among chromate workers in Germany. Gross and Kölsch (1943/44) reported eight more cases of lung cancer in three different chromate pigment plants. Baetjer (1950a, 1950b) reviewed the German and American literature on pulmonary carcinoma in chromate workers up to 1950 and concluded that 109 cases had been reported in workers employed in chromate-producing and 11 in the chromate pigment industry. She concluded that the incidence of respiratory

cancer among chromate workers was significantly higher than expected. Taylor (1966) and Bidstrup and Case (1956) have come to the same conclusion. Already in 1936 (Gross and Kölsch, 1943/44) German health authorities had recognized lung cancer as a possible occupational disease.

This paper reports a cohort study to evaluate the incidence of lung carcinoma in workers employed in a small company producing zinc-chromate pigment.

The company was established in 1948. From 1948 to 1951 production consisted of only lead-chromate pigment. From 1951 to 1956 both lead chromate and zinc chromate were produced; since 1956 the only product has been zinc chromate pigment. From 1948 to 1954 the number of employees varied from six to eight. Later the number has slowly increased to about 30 workers in 1972.

Today the company consists of three plants at

different locations some miles apart. One plant (C, Table 1) was built in 1972 with modern equipment and with production in a nearly closed system. The other two plants (A and B) are located in buildings previously constructed and used for herring-oil production and are consequently not suitable for the production of zinc chromate.

Methods

Chromate exposure was estimated by using portable pumps connected to membrane filters during a period of five working days for each of eight working areas within the three plants. The filters were treated with hydrogen fluoride in Teflon bombs (Langmyhr and Paus, 1968), and chromium was determined by the Perkin-Elmer atomic absorption standard method. All present employees were given a clinical examination including determination of vital capacity and forced expiratory volume in one second. Blood and urine were sampled for chromium determination. In this paper only the respiratory cancer incidence will be discussed and the present dust exposure values for the workers reported.

The company provided a list of 133 workers. This was a complete listing of all workers who had ever been employed in any of the three plants during the years 1948 until the end of 1972. Date of birth, address, and dates of starting and ending employment were included in the list. This information enabled identification of all cases of cancer which had occurred in the group since 1953 as registered by the Cancer Registry of Norway (1972). This information also enabled identification of workers with more than three years of exposure to chromate dust, as only these, a total of 24 men out of 133, were included in the cohort.

The Cancer Registry, established in 1951, has for 1953 and subsequent years presumably complete information of all cases of cancer diagnosed in Norway. For each calendar year during the defined period the Registry has available information of all deaths in Norway, including time of death and underlying and contributory causes.

For interpretation of the observed number of lung cancers among the employees as a health hazard, it was necessary to estimate how many cases of lung cancer would have been expected as normal in the group during the observation period. In this context normal denotes the risk encountered by the workers if their specific work and the risk of getting this particular disease were unrelated. The comparison of the observed number of cancers in the group with the expected number was made according to the method described by Pedersen, Høgetveit, and Andersen (1973). This method includes calculation of the risk of getting lung cancer for each worker separately for each calendar year of the observation period. This is done by using the age-specific incidence rates of cancer as supplied by the Cancer Registry. The total risk for the population of workers is then obtained by adding together the risk for each worker for each year of the observation period. The expected number of cases of cancer obtained by this method is then compared to the observed number in the group.

The analysis was confined to men who had been employed for at least three years in any of the three

plants, as this was taken as three years of exposure to chromate dust. Thus, for estimating the normal risk, cancer incidence risk for the years 1951 to 1972 had to be used. The Registry has these figures for each year during the period 1955 to 1971, and for this investigation, the figure for 1955 was used for the years 1951 to 1954, and the figure for 1971 was used for 1972. We could thus consider the workers with at least three years of exposure to chromate dust under observation from the beginning of 1951 to the end of 1972. Summation of individual risks was started at the beginning of the fourth year of employment. The risk was counted from 1 January the same year if employment started before 1 July and from 1 January the next year if employment started after that date. The risk was counted to the end of the year in which the lung cancer was diagnosed or to the end of the year of death, whichever was the earlier.

As the Registry has all information stored on magnetic tapes, the sum of individual risk factors, the normal risk for the group of workers, and the risk ratio were given directly, as reported under results. The Registry also reported that the cancer incidence rates in the county where all three plants are located is slightly lower than the national incidence rates used for estimation of normal risk.

Results

The total amount of dust in the plants ranged from 9.8 mg/m³ for the worker filling sacks in plant B to 1.2 mg/m³ for the corresponding operator in plant C (Table 1). The 95% confidence intervals of the measurements (assuming log normal distribution) were 5.0 mg/m³ to 13.6 mg/m³ and 0.9 mg/m³ to 1.7 mg/m³, respectively. The concentration of chromate as chromium in the air varied from 1.35 mg/m³ to 0.01 mg/m³. Sackfilling in plant C resulted in the lowest exposure level measured. Sackfilling in plant A and mixing raw materials in plants A and B gave eight hours' exposure levels for individual workers in the range of 0.3 to 0.4 mg Cr/m³. Sackfilling and mixing raw materials were generally the most dusty operations. The exposure of the foremen moving around in the plants was taken as a measure of general exposure for workers not exposed in particularly dusty operations.

All cases of cancer of all sites among the 133 workers listed by the company are shown in Table 2.

The cases of bronchial carcinoma were diagnosed in workers 41, 51, and 59 years of age, and all had been employed for more than three years.

The expected number of lung cancer cases in the cohort was calculated to be 0.079 cases for the total period of observation. As three cases were found, the observed/expected ratio was approximately 38. The total number of man-years-at-risk of the cohort was 244.

The exposure time of the workers was from four to 19 years, more than half being exposed for six years or less. Six of the 24 workers had an exposure time of four years only.

TABLE 1
CHROMIUM EXPOSURE IN DIFFERENT WORK OPERATIONS

Plant	Work operation	No. of days ¹	Mean values of total dust (mg/m ³)			Cr (mg/m ³)
			Xmin ²	$\bar{x}$	Xmax ²	
A	Sackfilling	5	5.0	6.3	10.2	0.43
	Mixing raw materials ..	4	2.4	6.0	12.6	0.35
	Foreman (all departments)	5	2.4	3.8	4.8	0.19
B	Sackfilling	5	5.0	9.8	13.6	1.35
	Mixing raw materials ..	5	3.1	3.5	4.7	0.33
	Foreman	5	1.4	1.9	2.3	0.04
C	Sackfilling	5	0.9	1.2	1.7	0.08
	Mixing raw materials ..	5	1.2	2.9	5.1	0.01

¹No. of measurements for average daily distribution

²95% confidence intervals with log normal distribution

TABLE 2
CASES OF CANCER AMONG 133 MEN
BETWEEN 1953 AND 1971

Site of cancer	No. of cases
Bronchus	3
Prostate	1
Gastrointestinal (pancreas) ..	1
Nasal cavity	1

If five years' exposure time had been taken as the minimum for introduction to the study, the cohort would have consisted of only 14 persons. The expected number of lung cancer cases would then have been approximately 0.035. As all three workers with bronchial carcinoma had an exposure time longer than five years, the observed to expected ratio in this case would have been 83.

The adenocarcinoma of the prostate was found in a worker who did not qualify for membership of the cohort. The gastrointestinal cancer was diagnosed in a man who had been employed for four years (1954/57). In this case the tentative diagnosis of cancer was based on clinical examination (large metastatic liver) and on cytological examination of ascites showing adenocarcinoma. The man died in 1972 and necropsy was not performed.

The single case of cancer of the nasal cavity was diagnosed in 1973 in a 33-year-old man who had been employed in the plant for only three months in 1970. This case is mentioned because the first case of cancer in a worker exposed to chromium was reported to be an adenocarcinoma of the inferior turbinate of the nose. The histological diagnosis in our case was adenoid cystic carcinoma.

Case reports of bronchial carcinomas

Case 1 Male, born in 1908. His employment lasted for six years (1949-54) until production in this particular plant was discontinued. He was exposed to both lead and zinc chromate pigment. In his hospital report there are no notes about smoking. After discontinuing his employment at the plant he worked as a joiner in various jobs. Before 1949 we have indications that he was a fisherman. He was admitted to hospital in January 1968 and died in February 1969. An anaplastic small-cell carcinoma of the left main bronchus was diagnosed.

Case 2 Male, born 1912. He was employed by the company from the middle of 1954 until the end of 1961. He worked in plant A, mostly in the sackfilling department, but was also involved in the manual mixing of raw material (sodium dichromate and zinc-white). He had been a heavy smoker for about 20 years. Before his employment at the factory he had a job on a ferry. From 1962 he worked as a warehouse assistant at a woodware shop. In September 1963 an oat-cell carcinoma of the lower right bronchus was diagnosed, and he died in February 1964.

Case 3 Male, born in 1931. Employment started at the beginning of 1956. He was doing much the same work as case 2 at the same plant (A). Since 1964 he has been doing mainly outdoor transport work for the company, probably with an insignificant exposure to chromate dust. Before 1956 he was a sailor. Since 1956 he has smoked 10 to 15 cigarettes a day. In October 1972 a tumour of the right lower lobe was diagnosed. The histological diagnosis was highly differentiated carcinoma. The patient was still alive at the end of 1973.

Discussion

This investigation has revealed an increased incidence of bronchial carcinoma among employees in a small zinc chromate producing company. The workers have been exposed to chromates as both the pigment and its raw material, sodium dichromate. In a small plant like the present the workers rotate and few of

the men can be classified by one specific job. It is known, however, that the cancer cases 2 and 3 above had operated the sack-filling equipment most of the time. The air analyses show that by far the highest chromate-dust concentrations in air are found in this working area.

Most of the cases of respiratory cancer previously reported with chromate exposure have been found in workers employed in the chromate-producing industry and only a few cases have been reported from the chromate pigment industry (Baetjer, 1950a). It is, of course, impossible to rule out sodium dichromate as a causative agent in our cases, but the results indicate that there is a cancer hazard also in connection with exposure to chromate pigments.

The exposure time to hexavalent chromium in these three cases has been six years in one case and eight years in the other two. The latency period from the beginning of exposure to chromate dust before bronchial cancer was diagnosed was 19, 9, and 17 years, respectively. This corresponds well with earlier observations (Baetjer, 1950a, b; Bidstrup and Case, 1956; Grushko, 1961). The average age of the three workers affected was 50 years, while the cohort includes all ages. If all workers above 60 years were excluded from the cohort, the observed to expected ratio would have been approximately 100 with more than three years of employment and much higher with more than five years. In the last case, however, the cohort would become too small to reach any conclusions. It is remarkable that two of the cancers have been found in relatively young persons.

The level of exposure to chromates in plants A and B for both the sackfilling and mixing procedure is clearly too high. Ventilation has been altered in the plants during the period of production, but the amount of pigment produced has increased. It is thus difficult to estimate previous exposure, but interviews indicate a level of the same magnitude as today.

It is difficult to judge to what extent the smoking habits of two of the three affected workers may have contributed to the development of their lung cancers. An interaction of the effect of the two different carcinogenic exposures certainly has to be considered. In plant B, where production was started in the middle of 1965, no cases of bronchial cancer have been observed so far. In this plant no one had been exposed to chromate dust for more than 7.5 years by the end of 1972.

The cohort will be followed up at regular intervals in the future. The results of the clinical examinations and exposure parameters based on blood and urine analyses will be published elsewhere.

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