

## Lung cancer in Japanese chromate workers

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**Ohsaki, Y., Abe, S., Kimura, K., Tsuneta, Y., Mikami, H., and Murao, M. (1978).** *Thorax*, 33, 372-374. **Lung cancer in Japanese chromate workers.** We have treated ten patients with lung cancer among workers in a chromate factory between 1972 and 1976. Four further cases were also found through death certificates and medical records. Most were smokers and all were men. The average duration of exposure to chromate was 24 years (range 10 to 36). The cell type in our ten patients was squamous in seven and small anaplastic type in three. The primary sites were all in large bronchi. The incidence (person per year) calculated from the number of employees, duration of factory activity, number of cancer patients, and shortest duration of labour period among the patients was 657.9 per 100 000 compared to 13.3 per 100 000 in Japan as a whole.

The first two cases of lung cancer among chromate workers were reported in Germany in 1911 and 1912 (Hueper, 1966). Spannagel (1953) reviewed 86 cases of lung cancer in chromate workers in Germany reported for the period 1911-52. The same type of cancer in chromate factories was recognised in America by Hueper (1966) and in England by Bidstrup (1951) and by Bidstrup and Case (1956). As a result of these studies, lung cancer among chromate workers was recognised as an occupational disease. However, there has been no such report from Japan, although chromate industries were present in several areas of the country. We noticed a high incidence of lung cancer among workers in a chromate factory in 1972 and now report the cases that occurred between 1972 and 1976, including those that were found through death certificates and medical records.

### Subjects

We diagnosed ten cases of bronchogenic carcinoma among workers from a chromate factory during 1972-6. In addition to these, four cases of lung cancer were found by studying medical records and death certificates of employees of the factory (see Table). All were men. Ages ranged from 27 to 67 years (average 50.3). The period of exposure to chromate dust ranged from ten to 36 years (average 24.8). All but two patients were heavy smokers. Initial symptoms were haemoptysis in

three patients, cough and expectoration in six patients, wheezing in one, and gait disturbance in one. The remaining four patients had no specific complaints concerning the respiratory tract, and lung cancer was found on routine examination of the workers. Diagnosis of cases found by medical record was based on a compatible clinical course and chest radiography. Details of cell type or primary site were limited to the ten patients whom we diagnosed, as this information was lacking in the four patients found by medical record. The histology was squamous cell carcinoma in seven and small cell carcinoma in three. No adenocarcinoma has yet been found. The primary site of the cancer was in the large bronchi in all ten patients. The tumour occurred in the left lower lobe bronchus in six patients, in the left upper lobe bronchus in three patients, and in the right lower lobe bronchus in one patient. None of the 14 patients had been exposed to atomic radiation.

### The factory and its employees

The factory was located in the centre of Hokkaido island, about 50 km from Sapporo city. The activity of the factory began in 1936 and ended in May 1973. The main products of the factory were chromic acid, sodium dichromate, and potassium dichromate. Taking the process of potassium dichromate as an example, chrome ore was combined, ground, and sintered with sodium

Table Chromate workers with lung cancers

Sex	Age	Labour period (years)	Smoking history (pack years)	Nasal perforation	Initial symptoms	Cell type
*M	27	10	10	?	Cough	Small cell anaplastic
*M	56	31	37.5	?	Blood-stained sputum	?
*M	40	25	?	?	Cough sputum	?
*M	56	30	0	?	Gait disturbance	Squamous
M	57	26	20	(+)	Cough sputum	Squamous
M	59	24	45	(+)	Cough sputum	Squamous
M	41	13	7.5	(+)	Blood-stained sputum	Small cell anaplastic
M	49	26	37.5	(+)	Cough fever	Squamous
M	67	14	37.5	(-)	Blood-stained sputum	Small cell anaplastic
M	57	36	30	(+)	Wheezing	Squamous
M	54	22	20	(+)	(-)	Small cell anaplastic
M	64	10	60	(-)	Cough sputum	Squamous
M	50	25	37.5	(+)	(-)	Squamous
M	59	28	30	(+)	(-)	Squamous

\*Detected from records.

carbonate and caustic lime. The product was percolated with water, then sodium dichromate was produced by adding sulphuric acid. Separation and crystallisation of sodium dichromate was performed and potassium dichromate was produced by adding potassium chloride (see Figure). It is clear from the flow chart of the process of dichromate production that there is a danger of producing several noxious dusts or mists, such as from ore, sodium carbonate, lime, sulphuric acid, monochromate, and bichromate, in the work places. The factory had old-fashioned equipment and made little attempt to prevent exposure of workers to noxious agents. The workforce numbered 67 men when the factory was closed on 31 May 1973, to which were added 487 retired workers, a total number of 554. The number of employees who had worked for longer than ten years, the shortest exposure period among the lung cancer patients, was 133. Based on this number, number of cancer patients, and period of the factory activity for 16 years from detection of the first case, calculated incidence (person per year) turned out to be 657.9 per 100 000 population

$$\text{(incidence} = \frac{\text{total cases over 16 years}}{\text{population at risk} \times 16} \times 100\,000).$$

This compares with a death rate in Japan in 1975 of 13.3 per 100 000 from bronchial carcinoma.

### Discussion

The high incidence of lung cancer among chromate workers has been reviewed in the report by Spanagel (1953). In addition to the non-chromic dust,

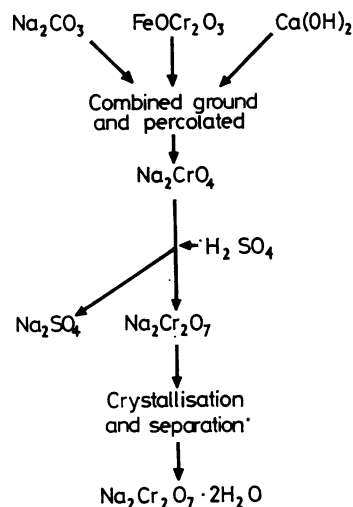


Figure Flow chart of sodium dichromate production process from chromium ore.

such as lime and sulphuric acid, these workers are also exposed to insoluble chromate containing trivalent chrome and soluble chromate containing hexavalent chrome. It is the popular belief that the main carcinogenic activity is due to hexavalent chromium. However, Machle and Gregorius (1948) incriminated monochromate as a carcinogenic substance as many lung cancer patients were detected in a factory handling monochromate only, compared with the relatively low incidence of lung cancer in a dichromate handling factory. According to Mancuso and Hueper (1951),

exposure to insoluble chromium, such as chromic dust and chromic oxide, may also play a part in carcinogenesis. Cancer of the skin or nasal passage is observed rather uncommonly, though burns of the skin and nasal septal perforation induced by soluble chromate in chromate workers occur more frequently. Our factory made final products from ore by operating many different processes. The factory was small and had old-fashioned equipment, so that the workers were often exposed to various noxious agents. Eight of our ten patients had nasal perforation as evidence of exposure. Baetjer (1950) reported 17 cases of nasal septal perforation in 22 patients.

The exposure period to chrome before lung cancer occurs has varied in different countries—from four to 47 years. Average duration was 17 years in America and 27 years in Germany (Baetjer, 1950). In our cases the average period was 24 years, ranging from ten to 36 years. Taking ten years, which is the shortest exposure period of our patients, 3 of 39 German cases and 13 of 49 American cases developed lung cancer in this period, indicating early occurrence of lung malignancy in America. The length of exposure periods before lung cancer develops would depend on the concentration and type of noxious agents, working conditions, and individual differences. According to Hueper (1966), chromate-induced lung cancer does not exhibit any special preference for any particular part of the lung. However, the primary site of the tumour was so limited to the large bronchi in our patients that the first symptoms, signs, and chest radiographic findings were often those of obstructive pneumonia. It is our policy to investigate even minor respiratory symptoms by exfoliative cytology of sputa, bronchoscopic examination, and bronchography in high-risk groups such as chromate workers. A chest radiograph may not detect carcinoma in the proximal parts of the main bronchus, while early detection of in-situ carcinoma of hilar type is only possible by cytology and bronchoscopy. The reported histological type of carcinoma in chromate workers has been predominantly squamous or anaplastic, amounting

to 112 in a total of 123 cases. The remaining 11 cases showed adenocarcinoma (Hueper, 1966). We found no adenocarcinoma. The carcinogenic mechanism of chromate compounds is not yet clear, nor is the relationship between smoking, chromates, and lung cancer. There were many heavy smokers among our cases. Even taking into account the smoking factor does not explain the incidence of lung cancer in chromate workers. Animal experiments have shown cancers produced by chromium compounds (Payne, 1960). Smoking is probably an accelerating factor on chromate hazard.

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