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Mortality Among Cadmium and Nickel-Exposed Workers in a Swedish Battery Factory†

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This cohort study comprised male workers who had been employed in a cadmium–nickel battery factory in Sweden. The subjects had been exposed to cadmium for more than 1 year between the years 1940 to 1980.

Of a total of 528 exposed workers, 525 were traced. The observed number of deaths due to various diseases was compared to the expected number, calculated from national statistics.

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Between 1951 and 1980, 105 men died before the age of 80, compared to an expected number of 122. In a subgroup of workers, totalling 185 men, who were exposed for more than 15 years, 51 died compared to an expected number of 58. There was a significant increase in deaths from nephritis and nephrosis (three observed, 0.4 expected). Furthermore, nonsignificant increases were observed for cancer of the prostate (three observed, 1.6 expected), urinary bladder cancer (two observed, 0.4 expected), and pulmonary cancer (three observed, 2.5 expected). One case of cancer of the nasopharynx was recorded.

KEY WORDS: Cadmium, nickel, occupation, battery factory, male workers, mortality, kidney disease, lung disease, cancer.

INTRODUCTION

At the end of the 1940's Friberg[1] showed that occupational exposure to cadmium can cause kidney and lung disease. These early observations on chronic health effects from cadmium have since been verified in several studies and have been discussed in major reviews.[2-4] The cadmium-induced kidney damage at an early stage is characterised by a particularly increased excretion of low molecular weight proteins in urine. This is a sign of renal tubular dysfunction and urinary β_2-microglobulin is a good indicator of this effect. In more severe cases, a generalised protein-uria, glycosuria and calcuria may develop.

In the worst cases, the cadmium-induced kidney dysfunction develops into glomerular damage and uremia. The increased excretion of calcium in the urine can also lead to renal stones. Occupational exposure to cadmium may also give rise to emphysema. In Japan, cadmium pollution of rice has caused a serious bone disease, Itai-itai disease, which is a combination of renal tubular damage, painful multiple fractures and osteopoenia (osteoporosis and osteomalacia). Among workers with long-term occupational exposure to cadmium, occasional cases of osteomalacia in combination with renal damage have also been described.

Six extensive epidemiological investigations of the mortality and cancer morbidity among cadmium-exposed workers have been published. In three of these an increased incidence of prostatic cancer is reported.[5-7] In one of these studies[6] there was also an increased risk of lung cancer.

Three more recent epidemiological investigations from the United Kingdom[8-10] do not report any increased mortality of prostatic

cancer or lung cancer. Holden[8] studied a copper smelter and Sorahan[9] studied a nickel–cadmium battery factory. Armstrong and Kazantzis[10] reported results of mortality from another 17 industries with cadmium exposure in the United Kingdom. No increase in the cancer risk was found. There was however a significant hypermortality in chronic obstructive lung disease among the cadmium workers. A previous and more extensive report by Armstrong and Kazantzis[11] is of interest since it also included data from the two cadmium industries earlier studied by Holden[8] and Sorahan.[9] In this report[11] it is evident that in both the smelter and the battery factory there was a non-significant hypermortality in prostatic cancer (nine observed cases as compared to 4.7 expected in the copper smelter, and four observed cases as compared to 1.7 expected in the battery factory). A non-significant tendency for a hypermortality in lung cancer, 26 observed as compared to 19.9 expected, also occurred in the battery factory.

The suspicion that cadmium can cause cancer is supported by animal experiments. Takenaka *et al.*[12] has shown that rats exposed to cadmium chloride in air at concentrations between 0.012 and 0.05 mg/m^3 for 18 months developed lung cancer at a high incidence, while no cases were found in a group of control rats. It has further been shown in several studies that repeated injection of cadmium can cause sarcoma at the site of the injection. In some cases these give rise to metastases.

Most of the epidemiological studies have mainly been aimed at showing the possible increases in cancer due to cadmium exposure. It should be pointed out though that at least in three of these reports there is an obvious hypermortality in certain non-malignant diseases, which probably is associated with cadmium. For instance, Holden[8] reports that among 347 workers, exposed to cadmium fumes in the smelter, there were 36 deaths due to lung disease, when the expected number was 20.3. Similar hypermortality in lung disease was observed by Kjellström *et al.*[7] among Sewdish workers and by Armstrong and Kazantzis.[10,11] An increased mortality in kidney disease has also been found[7,8] but these diseases are more unusual as the main cause of death even among cadmium workers with very heavy exposure. Nickel has mainly been reported to give effects in the lung. Experimental studies in rabbits have shown that inhalation of metallic nickel at levels above 0.1 mg/m^3 may cause certain

histopathological changes in the lung.[13] These are similar to those found in humans in the rare disease "pulmonary alveolar proteinosis". Epidemiological studies of the mortality among nickel-exposed workers has shown that exposure to nickel compounds with low solubility (e.g. the sulphides) increase the risk of lung cancer and nose cancer.[14]

This report includes results of an epidemiological study of the mortality among male workers in a Swedish nickel–cadmium battery factory (NIFE Jungner AB, Oskarshamn). The target group contains several od the workers studied by Friberg in the 1940's.[1] It is an extension and continued follow-up of the preliminary study earlier reported by Kjellström *et al.*[7]

MATERIAL AND METHODS

From the company, information was received about all employees who had been exposed to cadmium for longer than 1 year, in the period 1940 to 1980. A total of 545 men and 102 women were identified. As the female part of the cohort was young, and in general only exposed to cadmium for short periods during the last years, they were excluded from the present analysis. Seventeen of the men had emigrated and were thus excluded. Of the remaining 528 everybody except three could be identified either as dead or alive through the parish books and state insurance company files. This analysis therefore includes 525 men, who have been employed for at least 1 year since 1940. Many had, in fact, started their employment before 1940 (Table I).

TABLE I
Decade of employment for 525 battery workers.

–1920	1921–30	1931–40	1941–50	1951–60	1961–70	1971–80
23	47	46	138	67	145	59

Copies of the death certificates were received from the National Statistics Bureau. The official main cause of death was accepted, except in one case, where a misclassification was obvious. The expected number of deaths in different causes of death has been

estimated by multiplying the number of person years of follow-up with the age-, cause of death-, and calendar year-specific death rates for men in the whole of Sweden. Good statistics of causes of death in Sweden are only available after 1950, so the follow-up period was limited to 1951–1980. The analysis in this report has been limited to persons dying before age 80, as the cause of death data tend to be uncertain at higher ages. In the calculation, the computer system EPILIN at Linköping University has been used.[15] The p values have been calculated based on a Poisson-distribution. Two-sided tests have been used for testing of statistical significance.

EXPOSURE

The cadmium exposure levels in the factory were very high before 1950, often close to or in excess of 1 mg/m^3. After that the air levels of cadmium have decreased successfully. Since 1977 the Swedish hygiene standard of 0.02 mg/m^3 has seldom been exceeded. Workers have at the same time been exposed to nickel at about 5 times higher levels than the cadmium levels. The exposure situation in the factory has been reported and discussed in detail by Adamsson–Hassler.[16,17]

It has not been possible to calculate the individual dose, so this has been defined on the basis of the years of duration of exposure. Obviously 1 year of exposure duration in the beginning of the follow-up period would cause a many times greater dose than a 1-year exposure in the latter part of the follow-up period.

Individual workers' exposure duration varied between 1 and 52 years, with a median of 10 years. A quarter of the workers had an exposure period in excess of 22 years which means that they were heavily exposed both to cadmium and to nickel during some period.

RESULTS

A total of 105 workers had died before age 80 compared with an expected number of 122 (Table II). Excluding the workers with less than 15 years' exposure, the hypomortality becomes less pronounced, 51 observed deaths as compared to 58 expected. The deficit occurs in diseases of the cardiovascular system.

Calculations were carried out for many other combinations of

TABLE II
Observed and expected number of deaths before the age of 80 (1951–1980).

ICD No.	Cause of death	All workers ($n=525$)		Workers with at least 15 years of exposure ($n=185$)	
		Obs.	Exp.	Obs.	Exp.
1–999	All causes	105	122.0	51	58.2
140–209	All cancers	32	28.9	14	14.0
147	Naso-pharynx	1	<0.1	1	<0.1
150–151	Oesophagus-stomach	3	4.5	0	2.2
152–154	Intestines	6	3.5	2	1.7
157	Pancreas	3	1.8	1	0.9
162	Lung	6	5.0	3	2,5
185	Prostate	4	3.1	3	1.6
188	Bladder	2	0.9	2	0.4
390–458	Diseases of the circulatory system	47	57.1	21	28.5
460–519	Diseases of the respiratory system	5	5.1	2	2.5
490–493	Obstructive respiratory diseases	3	2.0	0	1.0
520–577	Diseases of the digestive system	4	5.7	4	2.6
580–607	Diseases of the genito-urinary system	4	2.5	4	1.2
581–584	Nephritis and nephrosis	3	0.9	3	0.4
800–999	Accidental death	10	11.7	4	4.4

exposure duration and latency periods, but these did not include any major differences compared to those presented in Table II.

In the sub-group with more than 15 years' exposure, there is a statistically significant hypermortality in chronic kidney disease. Three cases occurred whereas only 0.4 cases were expected (Table III).

A non-significant hypermortality also occurred for prostatic cancer (three cases as compared to 1.6 expected cases) and bladder cancer (two cases as compared to 0.4 expected cases). There was only a small difference in the number of deaths in lung cancer (three observed cases as compared to 2.5 expected cases). One case of cancer in the naso-pharynx, which is a rare type of cancer, had developed in a man with 12 years' exposure between the years 1933 and 1944. He died in 1972.

There was no tendency for an increased mortality in chronic obstructive lung disease in the group with more than 15 years'

TABLE III
Workers diseased with kidney diseases which could be related to occupational cadmium exposure.

ICD No.	Causes of death	Born	Died	Period of exposure
582	Nephritis with chronic uremia	1878	1952	1919–1944
582	Nephritis with chronic uremia	1899	1973	1919–1967
584	Nephropathy, chronic cadmium poisoning	1903	1968	1922–1950
592	Uremia, chronic cadmium poisoning, renal stones	1905	1967	1926–1956

exposure, but there was a non-significant hypermortality among those exposed to cadmium for less than 15 years (three observed cases as compared to 0.9 expected cases).

Scrutinizing the death certificates, revealed that one additional case of renal disease had occurred which most likely could be associated to former heavy cadmium exposure. The man died in 1967 after 30 years of cadmium exposure, and the immediate cause of death was cadmium induced chronic renal disease, uremia, and renal stones (classified according to ICD Code No. 592). There were also two cases of lung disease, which may be related to former occupational exposure. One worker with long-term cadmium exposure died in chronic interstitial pneumonia and another in pneumothorax, both unusual pulmonary diseases.

DISCUSSION

The study shows that the cadmium–nickel battery workers have had a lower overall mortality than expected when comparing with the national average mortality in Sweden. However, they had an increased relative mortality in chronic kidney disease, and possibly also an increased mortality for prostatic and bladder cancer and for workers with less than 15 years of exposure in chronic lung disease None of the latter increases were statistically significant.

The present results agree with those reported in earlier studies and this more complete analysis has not changed the general findings reported in the preliminary study by Kjellström *et al.*[7] An epidemi-

ological study of English workers in a nickel–cadmium battery factory has shown very similar results in a larger group of workers. Among those who have been employed more than one year, before 1980, 19 deaths in obstructive lung disease had occurred as compared to 13.1 expected cases. Eight deaths in nephritis–nephrosis had occurred as compared to 3.8 expected. Also in this study there was a non-significant hypermortality in prostatic cancer.[9,11]

There is only a very small difference between expected and observed mortality in lung cancer. The analysis of the mortality rates in lung cancer and other lung diseases should preferably be adjusted for smoking habits. Unfortunately, such data could not be collected for the deceased members of the cohort. A report from the occupational health care unit of the company in 1981 shows however that 53% of the cadmium–nickel exposed workers were smokers, 11% were former smokers and that 37% said they had never smoked. This frequency of smokers and past smokers is very similar for those reported for the whole of Sweden in the 1980's. There is therefore no indication that the smoking habits of the cadmium–nickel exposed cohort and the general population would be different.

In a number of cases renal disease and/or lung disease was mentioned in the death certificates as contributing to the cause of death. This observation could be a biased one, since the physician who wrote the death certificate in most cases was aware of his patient's former occupation. There is therefore an obvious risk that the physician exaggerates the importance of diseases which could be related to the former occupational exposure. It is nevertheless likely that in some cases the contributing disease is causally related to former occupational exposure. In this context it should be pointed out that the cadmium exposure for those workers who have died from renal disease and/or obstructive lung disease, which possibly could be related to cadmium, all except one had been employed before 1955 and thus were exposed to very high levels of cadmium.

The comparability with the national population average

The national average mortality rates do not constitute an ideal reference material for a group that has been working in industry. The data from the national averages includes unemployed, those who have various diseases to stop them from joining the labour market, those who live in institutions, the disabled people, etc. Such

groups have a higher mortality rate on average than the active working population. This leads to a lower mortality rate for most actively working cohorts than the expected rates based on the national mortality rates. The ratio between observed and expected mortality would therefore be expected to be in the range of 0.6 to 0.9 at ages below 70 years.[18]

The lower than expected mortality compared with the national average usually is most prominent for cardiovascular diseases. Such diseases often leads to symptoms that limit the worker's ability to continue at work. Those with heart disease therefore are less likely to join the actively working population and they may also have to leave work at an early stage because of the disease.[19] This well-known situation is also seen in the group of cadmium–nickel exposed workers. A great number of calculations were carried out on different subcohorts, e.g. for those who left employment before 1970 ("leaving cohort"). Different exposure duration and latency period criteria have also been used but no marked hypermortalities were seen except those reported in the tables.

The workers in this study had worked in the town of Oskarshamn. There are certain regional variations in overall mortality and cause-specific mortality in Sweden.[20] The south-eastern region of Sweden where this town is situated tends to have a lower overall mortality than the national average. The expected number of cases calculated from the national average mortality rates are therefore probably somewhat too high compared to the true expected mortality in this cohort. However, the regional variations are likely to be of less importance than, e.g. the "healthy workers effect" mentioned earlier.

CONCLUSIONS

The Swedish workers exposed to cadmium and nickel in a battery factory have not experienced an increased overall mortality as compared to the national average mortality data. Those with the highest exposure appear, however, to have an increased risk of dying in chronic kidney and possibly lung diseases, which agrees with earlier findings in a larger English study of cadmium–nickel battery workers. An increased mortality in bladder and prostatic cancer is also seen, but the increases are not statistically significant. Further studies on the cohort to increase the follow-up duration or to

increase the target population is needed to enable more definite conclusions as well as the use of a not cadmium exposed industrial cohort for reference.

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