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Cancer risk among workers at a copper/nickel smelter and nickel refinery in Finland

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Summary. A total of 1388 workers employed for at least 3 months at a copper/nickel smelter and nickel refinery were followed up for cancer from 1953 to 1987 through the Finnish Cancer Registry. There were 1339 male and 49 female workers, making a total of 27130 and 706 person-years, respectively. All of the women worked in the refinery, which opened in 1960, the same year the smelting of nickel began. A total of 67 cancers were diagnosed among the men, the standardized incidence ratio for all cancers being 1.0. No cancer was found among the women (1.8 expected). The risk of cancer among men was analysed according to primary site, exposure to nickel, type of work, years since first exposure and age at diagnosis. In the subcohort of nickel refinery workers, one case of sinonasal cancer was observed, against 0.02 expected, but otherwise no significantly increased risks of cancer were found. In addition to the small size of the cohort, the non-positive finding concerning lung cancer might be related to the relatively low arsenic exposure and, perhaps, to the late commencement of nickel production.

Key words: Arsenic – Cancer – Copper – Epidemiology – Nickel

Introduction

A thorough evaluation of the carcinogenicity of nickel has been recently published in the Monograph Series of the International Agency for Research on Cancer [4]. According to the expert group, nickel compounds are carcinogenic to humans, and metallic nickel may be carcinogenic to humans. All the epidemiological studies on cancer risk after nickel exposure were reviewed and most of them re-evaluated with an extended follow-up and more precise exposure data by the International Committee on Nickel Carcinogenesis in Man (ICNCM). The report of the ICNCM concluded that more than one form of nickel gives rise to lung and nasal cancer [6]. Besides nickel, smelter workers are also exposed to arsenic, which increases the risk of skin and lung cancer [1, 3, 4, 7].

The main aim of this study was to assess the risk of respiratory cancer among workers employed in nickel smelting and refining by a Finnish company since 1960. Those engaged in refining processes were primarily exposed to soluble nickel in the form of nickel sulphate. The workers involved only in copper production (employment ended before 1960) formed an internal comparison group. Nickel was the main carcinogenic agent in the environment; the smelter workers were exposed to very low levels of arsenic compounds until the late 1970s, because up to that time the smelter used ore from Finnish mines having an especially low arsenic content.

Subjects and methods

The study cohort was made up of workers at a copper/nickel smelter and a nickel refinery (Outokumpu Oy, Harjavalta Works) in southwestern Finland. Copper smelting started at Harjavalta in 1945. In 1949, electric smelting was replaced by the flash smelting method developed by the company. Nickel production commenced in 1960; the smelter was started up at the beginning of January and the refinery at the beginning of May. Since then the plant has converted nickel-copper ore to a high grade matte consisting of nickel-copper alloy, nickel subsulphide and copper sulphide. The later stages of copper production take place in another plant. The matte is ground, and then the nickel is extracted in a refining process involving atmospheric pressure leaching, electrolytic copper removal, cobalt removal and nickel electrowinning.

The exposure to nickel among the cohort members was defined by (a) period of employment and (b) area or type of work. Those workers whose employment had ended before the year 1960 had not been exposed to nickel. Nickel exposure among those still employed in 1960 or among those whose period of employment began later was largely dependent on the type of work. The workers were grouped into the following three categories according to work area or type of work: (1) smelter workers, (2) refinery workers and (3) maintenance staff. The maintenance staff worked, as necessary, in either of the two places. They were not continuously exposed to nickel compounds but underwent occasional, probably high, short-time exposures.

The exposure to nickel has been evaluated since 1966. The refinery workers were primarily exposed to soluble nickel compounds, mainly nickel sulphate and to a lesser extent nickel chloride (Table 1). As reported earlier [6], exposure levels at the Harjavalta Works have been low. Exposure to soluble nickel varied from 0.1

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Table 1. Description of the exposure of refinery workers to different forms of nickel at Harjavalta Works since 1960

Metallic nickel	In the form of metallic dust in the cutting and packing departments
Nickel sulphide matte	The high-grade nickel matte produced by the flash smelting process contains 60% nickel
Nickel oxides	Not present
Nickel hydroxide	Present at the cobalt removal stage in oxidation tanks. Since 1972, Ni(OH) has been the only insoluble form of nickel present in the electrowinning department. Exposure possible when dissolving tanks are cleaned or repaired
Nickel sulphide	Nickel matte and leaching precipitates contain NiS, but it is not present in the electrowinning department
Nickel subsulphide	Present in high concentrations in the nickel matte and in the air when the matte is ground. The airborne concentrations in the grinding hall are between 0.05 and 0.2 mg Ni/m^3. It is also present in the precipitates of the leaching reactors
Nickel chloride	Present in soluble form until 1972, concentrations have been low (not measured, however)
Nickel sulphate	Most of the nickel in the process and the air after leaching is in the form of soluble nickel sulphate
Nickel carbonyl	Not present
Nickel nitrate	Not present

to 0.5 mg Ni/m^3 (personal sampling) in the 1970s. The highest ever recorded single concentration in the electrowinning department was 1.1 mg Ni/m^3 (stationary sampling). Biological monitoring started in the late 1970s. Concentrations of nickel in urine in leaching workers after a working day were on average less than 0.85 µmol/l, whereas the concentrations in workers involved in the electrowinning process were on average 1.5–2 µmol/l.

The study population consisted of all workers who had been continuously employed at the Harjavalta Works (Outokumpu Oy) for at least 3 months during the period from January 1, 1945, to December 31, 1985. The cohort was formed using the company's employment records. The workers in the copper/nickel smelter and maintenance men were followed up for the incidence of cancer from 1953–1987 and those in the nickel refinery from 1960–1987. Workers who belonged to more than one exposure category were included in all of them in the analysis.

To study the risk of cancer related to nickel exposure, the workers were divided into two groups. Those whose employment ended before January 1, 1960, were not exposed to nickel. All employees who worked after that date were included in the nickel-exposed group. For these workers, the follow-up for cancer started from the date of the first nickel exposure (January 1, 1960, or the first day of employment, whichever came later).

Both the observed and the expected numbers of cancer cases were obtained from the files of the Finnish Cancer Registry. Follow-up commenced 3 months after the start of employment, and only cancers diagnosed between January 1, 1953, and December 31, 1987 (the closing date for the study), were accepted. The Registry covers virtually all cancer cases diagnosed in Finland during the study period [9]. The members of the cohorts were followed up for death and emigration, either through local population registers or by record linkage with the National Population Register. Eight workers (0.6%) could not be identified through the population registers and were excluded from the analysis. Another 7 employees had died before the beginning of the follow-up for cancer and were excluded. The final cohort consisted of 1385 employees. Two workers had moved abroad and were follwed up until the date of their emigration.

Table 2. Number of persons and person-years in the follow-up of the cohort of smelter and refinery workers from 1953–1987 in Finland by period of employment, type (site) of work and sex

Site of work	Employment ended before May 1, 1960		Employment continued or started after May 1, 1960[a]	
	No.[b]	Person-years[b]	No.[b]	Person-years[b]
Men				
Smelter	197	5172	566	10127
Repair shop	42	1178	238	4470
Refinery	–	–	369	6089
All men	233	6224	1106	19699
Women				
Refinery	–	–	49	706
Total	233	6224	1155	20405

[a] The starting date for calculation of the number of person-years at risk is either May 1, 1960, or the actual date employment started, whichever came later

[b] Some of the male employees had worked on two or three sites, and thus the numbers do not tally with those in the Total row

The expected numbers of cancers were calculated on the basis of person-years risk and with sex-, age-, and period-specific (5 subsequent 7-year periods) incidence rates for the population of southwestern Finland (a population of one million). The observed and expected numbers of cancer were also classified by follow-up year (0–4, 5–19, 20–). The standardized incidence ratios (SIR) were calculated by dividing the observed numbers of cancers by the corresponding expected numbers. The observed numbers are assumed to follow a Poisson distribution. The 95% confidence intervals for the SIRs were calculated from the tabulated confidence intervals of the Poisson mean [2].

Results

The 1339 men and 49 women in the cohort represented 27130 and 706 years of follow-up, respectively. The numbers of workers and years of follow-up by sex, exposure to nickel and site of work are presented in Table 2. Among the men, 67 cancers were diagnosed during the study period vs. 65.7 expected (SIR 1.0, 95% confidence interval, CI 0.8–1.3). No cancers were diagnosed among the women (1.8 expected). None of the risks for primary tumour sites was statistically significantly elevated (Table 3). There were almost no differences in the overall risk of cancer between those exposed to nickel and those who had not worked during the period of nickel production. The only exception is the one case of sinonasal (maxillary sinus) cancer among those exposed to nickel; the man who contracted the cancer had worked in the refinery for over 23 years.

Table 3. Observed (Obs) and expected (Exp) numbers and standardized incidence ratios (SIR) with 95% confidence intervals (CI) of cancers at selected sites among male workers at Harjavalta Works in Finland from 1953–1987, by exposure status (nickel production commenced May 1, 1960)

Site (ICD 7 code)	Employment ended before May 1, 1960				Employment continued or commenced after May 1, 1960, or later[a]			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All sites (140–204)	31	28.6	1.1	(0.7 –1.5)	36	36.0	1.0	(0.7 – 1.4)
Digestive tract (140–159)	10	8.2	1.2	(0.6 –2.3)	13	9.1	1.4	(0.7 – 2.4)
Stomach (151)	7	3.9	1.8	(0.7 –3.7)	5	3.7	1.3	(0.4 – 3.1)
Colon (153)	–	1.0	–	–	2	1.4	1.4	(0.2 – 5.0)
Respiratory tract (160–163)	9	9.2	1.0	(0.4 –1.9)	12	10.3	1.2	(0.6 – 2.0)
Nose and sinuses (160)	–	0.1	–	–	1	0.1	8.5	(0.2 –47.5)
Larynx (161)	1	0.7	1.4	(0.04–7.8)	1	0.8	1.2	(0.03– 6.7)
Lung and trachea (162)	8	8.3	1.0	(0.4 –1.9)	10	9.2	1.1	(0.5 – 2.0)
Bladder (181)	3	1.3	2.4	(0.5 –7.0)	–	1.7	–	–
Skin (non-melanoma) (191)	–	0.6	–	–	1	0.8	1.3	(0.03– 6.9)

[a] The starting date for calculation of the number of person-years at risk is either May 1, 1960, or the actual date employment started, whichever came later

Table 4. Observed (Obs) and expected (Exp) numbers and standardized incidence ratios (SIR) with 95% confidence intervals (CI) of cancer (all sites) among male workers at Harjavalta Works in Finland from 1953–1987, by site of work and period of employment (nickel production commenced May 1, 1960)

Site of work	Employment ended before May 1, 1960				Employment continued or commenced after May 1, 1960, or later[a]			
	Obs	Exp[b]	SIR	95% CI	Obs	Exp[b]	SIR	95% CI
Smelter	28	24.1	1.2	(0.8–1.7)	26	25.6	1.0	(0.7–1.5)
Repair shop	4	5.0	0.8	(0.2–2.1)	8	7.5	1.1	(0.5–2.1)
Refinery	–	–	–	–	6	5.4	1.1	(0.4–2.4)
Total	31	28.6	1.1	(0.7–1.5)	36	36.0	1.0	(0.7–1.4)

[a] The starting data for calculation of the number of person-years at risk is either May 1, 1960, or the actual date employment started, whichever came later

[b] Some of the employees had worked on two or three sites, and thus, the expected numbers do not add up to 28.6 and 36.0

Table 5. Observed (Obs) and expected (Exp) numbers and standardized incidence ratios (SIR) with 95% confidence intervals (CI) of lung cancer among male workers at Harjavalta Works in Finland from 1953–1987, by site of work and period of employment (nickel production commenced May 1, 1960)

Site of work	Employment ended before May 1, 1960				Employment continued or commenced after May 1, 1960, or later[a]			
	Obs	Exp[b]	SIR	95% CI	Obs	Exp[b]	SIR	95% CI
Smelter	7	7.0	1.0	(0.4 –2.1)	7	7.0	1.0	(0.4–2.1)
Repair shop	1	1.4	0.7	(0.02–4.0)	2	1.9	1.1	(0.1–3.9)
Refinery	–	–	–	–	2	1.0	2.0	(0.3–7.4)
Total	8	8.3	1.0	(0.4 –1.9)	10	9.2	1.1	(0.5–2.0)

[a] The starting data for calculation of the number of person-years at risk is either May 1, 1960, or the actual date employment started, whichever came later

[b] Some of the employees had worked on two or three sites, and thus, the expected numbers do not add up to 8.3 and 9.2

The overall cancer risk for male refinery workers did not differ from that of the other two groups exposed to nickel (Table 4). When the female workers were included in the analysis, the SIR of all cancers for the refinery workers was 0.8 (95% CI 0.3–1.8). The risk of sinonasal cancer for all refinery workers (both men and women) was significantly elevated (SIR 53.8, 95% CI 1.4–300). However, the risk estimate was based on only 1 case.

The risk of stomach cancer in the whole cohort was slightly elevated (12 observed vs. 7.8 expected), and the SIR was highest for the refinery workers (SIR 4.3, 95% CI 0.5–16). However, taking all the worker groups together (Table 3), the relative risk of stomach cancer was higher for those who had worked only in the copper smelter (SIR 1.8, NS) than for those who had been exposed to nickel (SIR 1.3, NS). The risk of lung cancer

was elevated only for the refinery workers (Table 5), and the SIR was not significant. No increased risk of non-melanoma skin cancer was found.

Workers exposed to nickel for 20 years or more had a higher relative risk of developing lung cancer (SIR 2.3, 95% CI 1.0–4.3) than those who had not been exposed (SIR 1.3, 95% CI 0.3–1.8). There was no trend in the SIRs by age. The workers under 30 years of age had a high risk of gastrointestinal cancer (2 observed against 0.14 expected).

Discussion

Our study evaluated the cancer risk for 1155 workers exposed to different amounts and different forms of nickel in a nickel refinery and copper/nickel smelter. Another 233 workers had been involved only in copper smelting. One part of the cohort had been described earlier without an analysis of the cancer risk, and the single case of sinonasal cancer was then reported [6]. According to the previous findings, the two types of cancers associated with nickel exposure are sinonasal cancer and lung cancer [5, 6]. In the present study, 1 case of sinonasal cancer was observed vs. 0.1 expected, and 10 cases of lung cancer were observed vs 9.2 expected among those exposed to nickel. The SIRs were not significantly elevated. The single case of sinonasal cancer occurred in a nickel refinery worker (0.02 cases were expected).

Since the closing date of the follow-up (December 31, 1987) 2 other cases of sinonasal cancer have been diagnosed, both of them among female refinery workers (in 1990 and 1991). The incidence data of the reference population are not yet available, but it is obvious that very high SIRs are to be expected.

An excess of sinonasal cancer had been found earlier among workers in the INCO refinery at Clydach (Wales), in the INCO sinter plant in Ontario (Canada), in the Falconbridge nickel refinery at Kristiansand (Norway) and in Huntington Alloys in West Virginia [6]. The greatest excesses were found in Clydach and Ontario among workers involved in processes which are no longer used. The exposure levels to soluble nickel were at least a thousand times greater than at present. The SIR found in our study has a wide confidence interval and is not readily comparable with previous risk estimates.

The association of nickel exposure with lung cancer seems to be weaker than that with sinonasal cancer [5]. However, in several cohorts exposed to nickel the risk of lung cancer was elevated [5, 6]. In the present study, the observed number of lung cancer cases among the 418 refinery workers was 2 as opposed to 1.0 expected. If the non-positive finding in our study is not due to the low exposure levels (assuming that nickel is a risk factor in lung cancer), there are two other explanations: the small size of the cohort (resulting in unstable point estimates of the SIRs) and the relatively recent commencement of nickel production (maximum follow-up 27 years). The risk of lung cancer for those who had been exposed to nickel and followed up for 20 years or more was significantly elevated (SIR 2.3, $P < 0.05$).

The ICNCM report [6] concluded that exposure to a mixture of oxidic and sulphidic nickel at very high concentrations seemed to explain most of the excess of respiratory cancer, but the exposure to large concentrations of oxidic nickel in the absence of sulphidic nickel was also associated with increased lung and nasal cancer risks [6]. The Harjavalta workers were not exposed to nickel oxides, but mainly to nickel sulphides and subsulphides in grinding and leaching processes, and to low concentrations of soluble nickel sulphates in the electrowinning department. On average, since 1966 when the monitoring started, the exposure level to soluble nickel (individual sampling) was less than 0.1 mg Ni/m^3 in the smelter and less than 0.5 mg Ni/m^3 in the refinery. Thus, these workers may indeed have been less exposed to carcinogenic forms of nickel than the workers in the cohorts evaluated previously. However, the 2 recently detected cases of sinonasal cancer (which could not be included in the analysis) indicate that even modest exposures to soluble nickel imply a significantly elevated risk.

Exposure to arsenic has been related to increased lung cancer risk among workers in copper smelters [1, 3, 5, 7]. One reason for the non-positive finding for the risk of lung cancer among smelter workers (14 observed against 14.1 expected) may be the low arsenic concentration in the ore. The ore used up to the late 1970s came from Finnish mines and has a very low arsenic content. From the beginning of the 1980s, the use of imported ore, and consequently arsenic exposure, has gradually increased.

The possible confounding effect of smoking could not be evaluated due to the lack of information on the smoking history of the members of the cohort. The differences in lung cancer incidence between occupational groups are largely determined by differences in smoking habits [8]. The prevalence of smokers is higher among industrial workers than in the whole population.

This study showed that the overall cancer risk among workers exposed to nickel was the same as in the reference population (36 observed vs. 36.0 expected). The non-positive result is only partly due to the healthy worker effect – during the first 5 years, follow-up of 2 cancers were observed, against 3.2 expected. The 3 cases of sinonasal cancer and the significantly elevated risk of lung cancer among those exposed to nickel and followed up for 20 years or more indicate that the risk of respiratory cancer even at moderate or low exposure levels is far from negligible.

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