

Cancer incidence among creosote-exposed workers

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KARLEHAGEN S, ANDERSEN A, OHLSON C-G. Cancer incidence among creosote-exposed workers. *Scand J Work Environ Health* 1992;18:26-9. Cancer incidence was studied among 922 creosote-exposed impregnators at 13 plants in Sweden and Norway. The subjects had been impregnating wood (eg, railroad cross-ties and telegraph poles), but no data on individual exposures were available. The study population was restricted to men employed during the period 1950-1975, and their cancer morbidity was checked through the cancer registries. The total cancer incidence was somewhat lower than expected, 129 cases versus 137 expected [standardized incidence ratio (SIR) 0.94]. Increased risks in both countries combined were observed for lip cancer (SIR 2.50, 95% confidence interval (95% CI) 0.81-5.83), skin cancer (SIR 2.37, 95% CI 1.08-4.50), and malignant lymphoma (SIR 1.9, 95% CI 0.83-3.78). Exposure to sunlight may have contributed to the risk of lip and skin cancer. The small number of cancer cases does not permit valid conclusions. The findings indicate that impregnating wood with creosote in earlier decades increased the risk of skin cancer.

Key terms: cohort study, impregnators, lip cancer, malignant lymphoma, skin cancer.

Creosotes consist of hundreds of compounds, and the main components identified are naphthalene and its alkyl homologues (1). Creosote oil is used as a preservative of wood. It is mostly used to impregnate railroad cross-ties and different types of poles (eg, telegraph poles).

The exposure may pose a risk of cancer, direct skin contact causing skin cancer (2, 3) and inhalation possibly increasing the risk for lung cancer (4). Information on such risks is available as case reports only. Case-referent studies have indicated increased risks for multiple myeloma (5) and for malignant lymphomas (6). A Swedish study based on census data observed an association between urothelial cancer and creosote (7). A review of the literature concluded, however, that data are too scarce to permit conclusions about this observation (8). Some compounds in creosote can be absorbed via the lungs and can be recovered from the urine of exposed workers (9).

For rats mutagenic activity has been demonstrated in urine after treatment of the skin with creosote, but no increase in mutagenic activity could be observed among creosote-exposed workers (10). In animal experiments cancer has been caused by mixtures of hydrocarbons similar to creosote (11).

A small study of 123 Swedish impregnators exposed to creosote and arsenic showed a small increase in mortality from tumors (12).

There has been public concern in both Sweden and Norway about the hazards from environmental exposure to creosote. The need for a comprehensive investigation in the two countries therefore became apparent. The aim of this cohort study was to investigate the cancer incidence and assess relative risks for different sites among impregnators in both countries.

Subjects and methods

The source population consisted of impregnators exposed to creosote at all plants known to have used creosote regularly; there were seven plants in Sweden and six in Norway. The personnel registers of the 13 plants listed all persons employed in 1950 and later.

The study base was restricted to men employed at least one year during the period 1950-1975, some of whom were hired before 1950. Only subjects with a verified exposure to creosote were included. Most of the subjects were impregnators, and 36 men employed by the Swedish Railway Corporation had been involved with the repair and maintenance of railroad cars designed to transport creosote. Two subjects were not included because of their unclear exposure status. In all, 352 impregnators from Sweden and 604 from Norway were recruited. Thirty-four subjects (3.6%) were excluded from the calculations because of missing data, 31 subjects due to missing identification numbers and three due to missing information on the year of hire. There was no reason to believe that these subjects differed from the others with regard to risk for cancer. The exclusion would therefore not have introduced an outcome-dependent selection. Consequently, the final study population included 346 Swedish and 576 Norwegian impregnators, totaling 922 subjects.

The degree of exposure to volatile carcinogens at the plants was not known. Creosotes have about 20 ma-

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major constituents with concentrations of more than 1%. Some of the constituents have proved to be carcinogenic, at least to experimental animals. Benzo[a]pyrene can be regarded as an indicator of carcinogenicity. The levels of naphthalene and diphenyl were measured in two of the Swedish impregnation plants, and the average concentrations were 2 mg/m³ and 0.07 mg/m³, respectively, peak concentrations occurring during the opening of cylinders and during the handling of wood before its drying (13). Similar concentrations were measured in two creosote impregnation plants in Finland (1). The average concentrations of vapors per workshift varied within the range 0.1–11 mg/m³. Naphthalene was the main component of the vapors. The concentrations of benzo[a]pyrene were lower than 0.03 µg/m³. Consequently, the average concentrations of each component were well below generally accepted exposure limits (14). The combined carcinogenic effect of volatile carcinogens was not estimated in either of the two studies already referred to. The exposure levels during earlier decades were probably higher.

Neither information on the individual exposure levels to creosote nor information on the individual smoking habits could be obtained in this study. A questionnaire on the type of work was completed by the management of all the plants. No significant differences in exposure conditions appeared. The impregnation started when the wood was placed in an autoclave containing creosote oil, which penetrated the wood when the air pressure in the autoclave was increased. When the wood was removed from the autoclave, the operator was exposed to creosote vapor. As the wood was handled manually, the skin of the operator was often exposed to creosote. Moreover, contamination of the skin occurred when the autoclave and the pipes were cleaned or repaired.

However, two of the Swedish plants used other wood preservatives as well — one used copper and

chromium salts and the other, with 29 employees, used arsenic in 25% of the total production volume.

In both countries cancer registration is based on compulsory reporting from clinical and pathological departments. The quality and coverage of the registration are considered to be good. All of the subjects in the cohort were checked through the registries of the two countries through 79 years of age. The follow-up period was 1958–1985 in Sweden and 1953–1987 in Norway. The difference in follow-up times was due to different periods of coverage in the two countries.

The person-years under risk within five-year age groups through 79 years of age were multiplied by the specific national cancer incidence rates for the expected number of cancer cases. The cancer registries provided the incidence rates, specific for gender, age within five-year age groups, calendar years, and cancer site. The person-years were calculated by use of modified life tables.

The standardized incidence ratio (SIR), that is, the relative risk, was calculated as the ratio between the observed and expected number of cancer cases. The standardization procedure used for the SIR was the indirect method. The calculations of exact 95% confidence intervals of the SIR values and the statistical significance of increased SIR values (one-tailed *P*-value < 0.05) were based on the assumption of a Poisson distribution of the observed cases.

Results

The total cancer incidence was somewhat lower than expected during the follow-up periods, 129 cases against 137 expected (table 1). Table 1 shows some differences in relative risks between the Swedish and Norwegian subgroups, but the observed numbers are

Table 1. Observed numbers of cancer at different sites for the Swedish and Norwegian subgroups — relative risks as the standardized incidence ratio (SIR). (95% CI = 95% confidence interval)

Site	Sweden			Norway			Total		
	Observed number	SIR	95% CI	Observed number	SIR	95% CI	Observed number	SIR	95% CI
Lip	1	1.80	0.04–10.0	4	2.72	0.74–6.97	5	2.50 ^a	0.81–5.83
Gastrocolorectal	6	0.63	0.23–1.37	23	1.07	0.68–1.60	29	0.93	0.62–1.33
Lung	2	0.36	0.04–1.30	11	1.00	0.50–1.79	13	0.79	0.42–1.35
Bladder	1	0.31	0.01–1.73	9	1.54	0.70–2.93	10	1.11	0.53–2.04
Prostate	6	0.66	0.24–1.44	13	0.74	0.39–1.26	19	0.71	0.43–1.11
Malignant melanoma	1	1.01	0.03–5.63	4	2.08	0.57–5.33	5	1.72	0.56–4.01
Nonmelanoma skin cancer ^b	6	4.17	1.53–9.10	3	1.28	0.26–3.75	9	2.37 ^c	1.08–4.50
Malignant lymphoma	3	1.90	0.39–5.55	5	1.90	0.62–4.44	8	1.90 ^d	0.83–3.78
Hodgkin's lymphoma	1	2.51	0.06–13.9	1	1.67	0.04–9.29	2	2.00	0.24–7.23
Non-Hodgkin's lymphoma	2	1.75	0.21–6.34	4	1.97	0.54–5.05	6	1.89	0.69–4.12
Leukemia	1	0.74	0.02–4.13	1	0.42	0.01–2.34	2	0.64	0.08–2.31
All sites	39	0.83	0.59–1.13	90	1.00	0.80–1.23	129	0.94	0.78–1.10

^a *P* = 0.05. ^b Basocellular skin tumors not included. ^c *P* = 0.02. ^d *P* = 0.06.

Table 2. Observed and expected numbers of selected types of cancer by time since first employment.

Site	Time since first employment					
	1–9 years		10–19 years		≥20 years	
	Observed number	Expected number	Observed number	Expected number	Observed number	Expected number
Lip	—	0.21	—	0.47	5	1.34 ^a
Nonmelanoma skin cancer ^b	—	0.21	3	0.65 ^c	6	2.94
Malignant melanoma	1	0.38	—	0.75	4	1.78
Lung	1	1.36	—	3.49	12	11.6
All sites	12	11.3	19	28.7	98	97.3

^a 95% confidence interval 1.21–8.7 ($P=0.01$).

^b Basocellular skin tumors not included.

^c 95% confidence interval 0.95–13.5 ($P=0.03$).

small, and therefore the differences for some sites may have arisen by chance. Increased risks were observed for lip cancer (SIR 2.50, $P=0.05$), nonmelanoma skin cancer (SIR 2.37, $P=0.02$), and malignant lymphoma (SIR 1.9, $P=0.06$).

Time since first exposure is of importance in most occupational cancer studies. In the group of workers with a latency period of 20 years or more, cancer of the lip showed an excess risk of 3.7 cases (5 and 1.34 observed and expected, respectively) (table 2). For non-melanoma skin cancer the excess risk was 3.1, and for malignant melanoma it was 2.2, the observed and expected numbers being 6 versus 2.94 and 4 versus 1.78, respectively. The next step in the analysis would be a further stratification by exposure in addition to the stratification by latency time. However, this analysis was not carried out due to the small numbers and lack of individual exposure data.

Discussion

In the present study workers exposed to creosote at impregnation plants in Sweden and Norway were found to have a decreased overall risk of cancer compared with that of the national male populations. An increased risk was however demonstrated for lip cancer and nonmelanoma skin cancer, especially after a latency period of 20 years or more.

Of the cancer sites primarily assumed to be associated with exposure to creosote, the lip and skin had increased cancer incidences, although only the latter was statistically significant. The increases could, at least in part, be explained by the creosote exposure, since skin contact must have occurred almost daily. The incidence of malignant melanoma was increased in the Norwegian subgroup only, 4 observed versus 1.92 expected cases. The numbers of the three different cancer sites together (ie, lip and skin cancer and malignant melanoma) amounted to 19 observed versus 8.72 expected cases, corresponding to an SIR of 2.18 (95% confidence interval 1.31–3.40, $P<0.01$). It would have been desirable to include the basocellular skin tumors in the study as well, but reliable information

on this tumor could not be obtained as the cancer registries did not have a complete report of these tumors. Reports of this tumor vary between hospitals and have also varied over periods of time.

The expected number of cases was based on national, not regional, rates. It could be questioned if this choice of reference could have introduced bias to the comparison. The base risk for cancer clearly differs both between various regions of the countries and between urban and rural areas. As to the variation between regions the plants were located in the southern and middle parts of the countries and not concentrated in one district. Even though the geographic distribution of the plants was not representative of national populations, it was considered to be wide enough to permit a comparison with the national rates. The variation in cancer rates between regions differs between cancer sites, and therefore it was not possible to find the ideal reference for the 10 sites examined in this study.

As to the difference in cancer rates between urban and rural areas, the use of national rates could well have introduced a bias because most of the plants were located in rural areas. Consequently, the relative risk of lung cancer may have been underestimated, and the relative risk of lip cancer overestimated by the use of national rates. However, the rates of cancer of the lip, malignant melanoma, and skin cancer pooled together do not seem to differ between rural and urban areas.

The impregnators had partly worked outdoors, and an increased risk of skin diseases caused by sunlight would be expected. It can therefore not be ruled out that exposure to sunlight contributed to the risk of lip and skin cancer. This possibility is supported by the findings of a review of epidemiologic studies on cancer morbidity among farmers (15).

No increase in the incidence of lung cancer (SIR 0.79) was observed although this cancer site is critical to exposure to volatile carcinogens. After a latency period of 20 years, 12 cases of lung cancer versus 11.6 expected were observed.

There was an elevated risk of malignant lymphoma in both subgroups, corresponding to an SIR of 1.9. Similar findings were reported for two Swedish case-

referent studies in which associations were observed between exposure to creosote and the risks of multiple myeloma (5) and malignant lymphoma (6). These two studies and the present Swedish subgroup share, however, the same study base (ie, they encompass approximately the same time period and the same geographic area). Therefore the findings cannot be regarded as independent. However, the fact that also the Norwegian subgroup showed an increased incidence, 5 cases versus 2.6 expected, supports a causal interpretation for this association.

No increase in the incidence of bladder cancer could be found. This result is contrary to the findings of a Swedish register-based study (7).

The probability of detecting an increased risk of cancer depends on the magnitude of the study base (ie, the number of person-years). The Norwegian subgroup comprised 16 200 person-years, and the Swedish one 8000 person-years. There was a sufficiently long period of follow-up for the induction of lung cancer. The probability of detecting a doubled incidence of lung cancer in this study cannot be calculated with certainty, but a crude estimate indicates that 10 000–20 000 person-years would be a sufficiently large study base to detect this or a larger risk with 90% probability at a 5% level (ie, $1-\beta=0.90$ and $\alpha=0.05$).

The smoking habits of the study population were not known. If the proportion of smokers in the study population differed considerably from that in the population in general, there would be an impact on the lip and lung cancer risks. However the large differences required are not likely to have existed (16). Throughout the study period preservatives other than creosote have been used, mainly mixtures of salts of copper, chromium, and arsenic. There are epidemiologic studies indicating that both skin cancer and lung cancer can be caused by inorganic arsenic compounds in medications and drinking water or by exposure to arsenic in smelting plants (17). However, no case of skin cancer was observed in the Swedish plant using 25% arsenic.

In conclusion, this cohort study of 922 Swedish and Norwegian impregnators showed a somewhat lower total cancer morbidity than expected. A doubled risk for skin cancer was however observed, and this increase could probably be attributed to the combination of exposure to creosote and sunlight. Valid conclusions about risks for other cancer sites can however not be drawn from the findings of this study.

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