

## SHORT REPORT

## Mortality and cancer incidence among Swedish lumberjacks exposed to phenoxy herbicides

Åke Thörn, Per Gustavsson, Jonas Sadigh, Brita Westerlund-Hännestrand, Christer Hogstedt

### Abstract

**Objectives**—To determine mortality and cancer incidence relative to exposure to phenoxy herbicides.

**Methods**—A cohort of Swedish lumberjacks of which 261 were exposed to phenoxy herbicides, and 250 were unexposed, was followed up for mortality from 1954 to 1994, and for cancer incidence from 1958 to 1992. The number of days of exposure to phenoxy herbicides was determined from pay slips. With the county population as a reference, standardised mortality ratios and cancer incidence ratios (SMR and SIR) were calculated.

**Results**—Mortality and cancer incidence were low with two exceptions; a small but highly exposed group of foremen showed an increased cancer incidence (SIR 274, 95% confidence interval (95% CI) 100 to 596), and over all mortality (SMR 141, 95% CI 68 to 260). Of three cases of non-Hodgkin's lymphoma, two were found among the most exposed workers.

**Conclusions**—The results provide some support to claims of previous studies that exposure to phenoxy herbicides might be related to non-Hodgkin's lymphoma and to an increased overall cancer risk.

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Keywords: phenoxy herbicides; lumberjacks; cancer

Phenoxy herbicides, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-dichlorophenoxyacetic acid (2,4-D), have been used world wide for weed control in agriculture and forestry. They have been associated with an increased overall risk of cancer, and increased risks of soft tissue sarcoma and non-Hodgkin's lymphoma.<sup>1</sup> They are often contaminated with polychlorinated dioxins, which in bioassays have been shown to be carcinogens.<sup>1</sup> In human carcinogenesis, however, the evidence for an aetiological role of phenoxy herbicides is inconsistent and controversial.<sup>2</sup>

In Sweden, phenoxy acids were used in forestry from the 1950s until the use of 2,4,5-T was totally prohibited in 1977. The use of 2,4-D in forestry was banned in 1983, and in all other sectors in 1990. In some Swedish for-

estry companies, the workers' use of phenoxy acids was registered for wage calculations. In such cases, good exposure estimates can be made. This mortality and cancer incidence study of lumberjacks at a Swedish forestry company, which used phenoxy acids during the period 1954-1967 has taken advantage of these good exposure estimates. In a previous study of this cohort,<sup>3</sup> its fate was followed up to 1978. The cohort has been expanded by the addition of the exposed female workers, and follow up time has been prolonged with the aim to determine mortality and cancer incidence relative to exposure to phenoxy acids.

### Subjects and methods

#### STUDY POPULATION

The source material consisted of records maintained by a Swedish forestry company. The study population comprised men and women, who were resident in Sweden and employed by the company at any time between 1954 and 1967. The number of working hours or days of the lumberjacks' different work tasks was noted on the pay slips. Those registered as exposed to phenoxy acids for more than 5 working days were referred to as an exposed subcohort, whereas those who had been registered as exposed to pesticides other than phenoxy acids and DDT were excluded from the study. Those who were not exposed to any type of pesticides were referred to as an unexposed subcohort. There were very few unexposed women, which is why they were excluded from the study. With these criteria, the final study population consisted of 514 people distributed in four subcohorts: 145 exposed male and 103 exposed female workers, 16 exposed foremen, and 250 unexposed male workers.

#### FOLLOW UP

The cohort was followed up for mortality from 1 January 1954, or from the start of employment, to 31 December 1994 in the National Register of Causes of Death. New cases of cancer were identified from the Swedish Cancer Register from 1 January 1958 (or from start of employment if later) until 31 December 1992, or until death if it occurred before that date. Death certificates with registered underlying cause of death were provided by Statistics Sweden. The life outcomes of three exposed and

Unit for Occupational Health, Sunderby Sjukhus, S-971 80 Luleå, Sweden  
Å Thörn

Department of Occupational Health, Karolinska Hospital, S-171 76 Stockholm, Sweden  
P Gustavsson  
J Sadigh

BeFris Läkarmottagning, Box 3105, 750 03 Uppsala, Sweden  
B Westerlund-Hännestrand

National Institute for Working Life, S-171 84 Solna, Sweden  
C Hogstedt

Correspondence to:  
Åke Thörn  
ake.thorn@nll.se

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Table 1 Cancer incidence (SIR) among exposed and unexposed subcohorts

Cancer diagnosis	Exposed					Lumberjacks, male (n=139) person-years=4079.2					Lumberjacks, female (n=103) person-years=3408.0					Unexposed lumberjacks, male (n=241) person-years=6694.0				
	ICD-7	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI			
																		Foremen (n=15*) person-years=345.3		
All sites	140-209	6	2.19	274	100 to 596	12	16.72	72	37 to 125	12	14.60	82	42 to 144	37	43.05	86	61 to 118			
Oral cavity	143-144	0	0.01	—	—	0	0.05	—	—	1	0.05	2000	26 to 11128	0	0.13	—	—			
Stomach	151	0	0.19	—	—	2	1.34	149	17 to 539	1	0.53	189	2 to 1050	2	3.78	53	6 to 191			
Colon	153	0	0.14	—	—	1	1.13	88	1 to 492	0	0.98	102	1 to 568	4	2.91	137	37 to 352			
Rectum and anus	154	0	0.12	—	—	1	0.89	112	1 to 625	0	0.53	—	—	3	2.39	126	25 to 367			
Liver primary	155	0	0.05	—	—	2	0.40	500	56 to 1805	0	0.40	—	—	1	1.05	95	1 to 530			
Pancreas	157	1	0.09	1111	15 to 6182	0	0.62	—	—	0	0.45	—	—	2	1.65	121	14 to 438			
Larynx	161	0	0.03	—	—	0	0.17	—	—	0	0.05	—	—	1	0.45	222	3 to 1236			
Bronchus and lung primary	162.1	1	0.24	417	5 to 2318	0	1.67	—	—	0	0.46	217	3 to 1210	5	4.34	115	37 to 269			
Prostate	177	2	0.43	465	52 to 1679	3	3.49	86	17 to 251	—	—	—	—	4	9.40	43	11 to 109			
Kidney	180	0	0.10	—	—	0	0.71	—	—	0	0.45	—	—	4	1.86	215	58 to 551			
Bladder	181	1	0.13	769	10 to 4280	1	0.98	102	1 to 568	0	0.26	—	—	1	2.53	40	1 to 220			
Melanoma	190	0	0.04	—	—	0	0.34	—	—	1	0.29	345	5 to 1919	0	0.71	—	—			
Other skin tumours	191	1	0.06	1667	22 to 9273	0	0.56	—	—	0	0.26	—	—	3	1.50	200	40 to 584			
Brain	193	0	0.06	—	—	0	0.49	—	—	0	0.45	—	—	1	1.09	92	1 to 510			
Unspecified of unknown site	199	0	0.09	—	—	0	0.69	—	—	0	0.62	—	—	3	1.76	170	34 to 498			
Haematopoietic tumours	200-209	0	0.19	—	—	1	1.46	68	1 to 381	1	0.84	119	2 to 662	3	3.56	84	17 to 246			
Non-Hodgkin's lymphoma	200	0	0.01	—	—	1	0.52	192	3 to 1070	1	0.33	303	4 to 1686	1	1.23	81	1 to 452			
Multiple myeloma	203	0	0.03	—	—	0	0.25	—	—	0	0.15	—	—	1	0.65	154	2 to 856			

\*One of the 16 foremen died before 1958, so for the cancer incidence study only 15 people were left at risk.

seven unexposed male workers could not be traced, and the subsequent analyses were based on 261 exposed and 243 unexposed lumberjacks.

#### EXPOSURE DATA

The notes on work types on the pay slips were interpreted with the aid of foremen, workers, and office personnel who had been employed during the period 1954-67. Phenoxy acids were used in two ways:

“Pocketing”—a groove was cut in the trunk of the tree, and the herbicide was poured into this cut “pocket”.

“Spraying”—a container with the herbicide was carried on the back. Up to the middle of the 1960s, it was sprayed with a manual pump and after that with a motor driven pump.

In pocketing, 3-6 l of concentrated herbicide were used per person and day, which corresponded to 1-2.5 kg 2,4-D salt and 0.2-0.3 kg 2,4,5-T salt. In spraying, the same total amount of herbicides was used, but the relation of 2,4-D and 2,4,5-T was 2:1. No information on possible contamination with dioxins exists.

Mean exposure time to phenoxy acids was 30 days working with spraying or pocketing (range 6-114 days) for the exposed workers and 176 days (range 1-317 days) for the foremen. All foremen and most (83%) of the exposed lumberjacks had also been exposed to DDT for a few years in the 1960s.

#### ANALYSIS

Standardised mortality and cancer incidence ratios (SMR, SIR) were calculated by the person-year method.<sup>4</sup> Expected mortality and cancer incidence were calculated from the death and cancer registers, with standardisation for age (5 year classes), calendar time (5 year classes), sex, and county. For the calculation, the computer programme OCMAP was used.<sup>5</sup> The 95% confidence intervals (95% CIs) of SMR and SIR were calculated with an exact method based on the Poisson distribution.<sup>6</sup>

#### Results

The total number of deaths in the cohort was below that expected in the region. For all men taken together, the SMR was 91 (95% CI 79 to 104), and for the women 70 (42 to 110). The number of deaths from diagnosed tumours was also lower than expected with SMR 88 (63 to 120) for men and 88 (35 to 181) for women. In fact, in all the subcohorts, death rates were below those expected regionally, with the exception of the foremen. This small (n=16) group showed an increased total mortality, SMR 141 (68 to 260) as well as an increased mortality from tumours, SMR 186 (CI 39 to 545) and from circulatory diseases, SMR 132 (43 to 307).

The cancer incidence was likewise lower than expected for the cohort as a whole. For all diagnosed malignant tumours, the SIR for the total male population was 89 (67 to 116) and 86 (61 to 118) for the women. In the subcohorts, the total cancer incidence was lower than expected, again with the exception

of the foremen, who had a significantly increased incidence, SIR 274 (100 to 596, table). Of the specific cancers, the finding of three cases of non-Hodgkin's lymphoma, two in the exposed and one in the unexposed subcohorts is noteworthy (table).

Mortality and cancer incidence were also calculated relative to total number of days in work with phenoxy acids as an indicator of cumulative exposure. For this, two levels were used; less than 26 days (below median exposure) and 26 or more days (above median exposure) in work with phenoxy acids. These calculations did not show anything but random patterns. However, both exposed cases of non-Hodgkin's lymphoma were encountered in the highest level of cumulative exposure to phenoxy herbicides, SIR 235 (29 to 850) where the expected number of cases was 0.85. They had been exposed for 114 and 45 days, respectively. The third case was found in the unexposed subcohort, where the expected number of cases was 1.23.

### Discussion

Many studies on the role of pesticides in the aetiology of human cancer have been published.<sup>1,2</sup> However, despite evidence from laboratory studies supporting a cancerogenic role for many pesticides, the evidence from epidemiological studies is weak.<sup>7</sup> A consistent increased incidence of all cancer in general has not been found. For individual or classes of pesticides linked to specific cancers, associations between exposure to phenoxy acids and non-Hodgkin's lymphoma and soft tissue sarcoma have been shown, even though the risks do not seem to be particularly increased.<sup>1,8,9</sup> Also, it seems as though they are mainly related to dioxin contamination.<sup>1</sup>

In the present study, a low total mortality and cancer incidence was the most conspicuous finding, which might depend on the selection of strong and healthy people to the demanding job of a lumberjack. Studies on the health effects of pesticides generally have two limitations: small study populations and imprecise exposure estimates.<sup>9</sup> The cohort of this report is small. However, its exposure was relatively well described for number of exposed

days, and the follow up of the people in the cohort was nearly complete (98%). Also, as the national cancer register is of high quality,<sup>10</sup> it does not seem likely that the absence of increased risks in the studied cohort and subcohorts would be due to defects in the study design or execution.

From the general pattern of decreased risks in the study results, there were, however, two important exceptions.

The first is the very small group of foremen, who had a significantly increased cancer incidence (table), and an increased overall mortality. This subcohort was substantially more exposed to phenoxy acids than all others, and had also been exposed to DDT for a few years.

The second consists of the two cases of non-Hodgkin's lymphoma (table) among the highly exposed male and female lumberjacks (SIR 235).

In view of earlier findings of an increased overall risk of cancer as well as of non-Hodgkin's lymphoma among lumberjacks,<sup>1,7-9</sup> these study results are worth bearing in mind. However, the associations are based on small numbers, and it is impossible to draw any conclusions on the aetiological connection between malignant disease and phenoxy acids.

- 1 Kogevinas M, Becher H, Benn T, et al. Cancer mortality in workers exposed to phenoxy herbicides, chlorphenols, and dioxins. *Am J Epidemiol* 1997;145:1061-75.
- 2 Maroni M, Fait A. Health effects in man from long term exposure to pesticides. A review of the 1975-91 literature. *Toxicology* 1993;78:1-180.
- 3 Hogstedt C, Westerlund B. Kohortstudie av dödsorsaker för skogsarbetare med och utan exposition för fenoxisyrpreparat. (A cohort study of the causes of death of lumberjacks with and without exposure to phenoxy acids.) *Läkartidningen* 1980;77:1828-30. (In Swedish.)
- 4 Breslow NE, Day NE. *Statistical methods in cancer research. Vol II. The analysis of cohort studies*. Lyon: International Agency for Research on Cancer, 1987. (IARC Sci Publ No 82.)
- 5 Marsh GM, Ehland J, Paik M, et al. OCMAP/PC: a user-oriented occupational cohort mortality analysis program. *American Statistician* 1986;40:308-9.
- 6 Bailar JC, Ederer F. Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics* 1964;20:639-43.
- 7 Zahm SH, Ward MH, Blair A. Pesticides and cancer. *State of the Art Reviews Occupational Medicine* 1997;12:269-89.
- 8 Weisenburger DD. Perspectives in pathology. Human health effects of agricultural use. *Hum Pathol* 1993;24:571-76.
- 9 Morrison HI, Wilkins K, Semenciw R, et al. Review. Herbicides and cancer. *J Natl Cancer Inst* 1992;84:1866-74.
- 10 National Board of Health and Welfare. *Cancer Incidence in Sweden 1993*. Stockholm: NBHW, 1996.