

Occupational factors and pancreatic cancer

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ABSTRACT The relation between occupational factors and pancreatic cancer has been studied by two different approaches: a population based case-control study with two series of controls and a retrospective cohort study based on register data. With both approaches, some support was found for an association with occupational exposure to petroleum products. Associations were also indicated with exposure to paint thinner (case-control study) and work in painting and in paint and varnish factories (cohort study), for exposure to detergents, floor cleaning agents, or polish (case-control study) and with floor polishing or window cleaning (cohort study), and for exposure to refuse (case-control study) and work in refuse disposal plants (cohort study).

Little is known about the aetiology of pancreatic cancer, but possible associations with occupational factors have been discussed.¹⁻³ Several chemical agents have been shown to produce pancreatic cancer in laboratory animals.⁴ Previous epidemiological findings have indicated excess risks of pancreatic cancer in several occupational groups, including chemists,⁵ wood related occupations^{6,7} and paper manufacturing,⁸ metal industries and aluminium milling,^{7,9} oil refining,⁸ and occupations involving exposure to gasoline.¹⁰

In the present paper we present the findings from an investigation of occupational factors and pancreatic cancer in Sweden, using two different approaches: a population based case-control study and a retrospective cohort study. The purpose was to investigate possible associations between pancreatic cancer and occupational factors, including exposures related to wood and paper, metal, and petroleum products.

Material and methods

The case-control study included all incident (newly diagnosed) cases of cancer of the exocrine pancreas in subjects aged 40-79 at three surgical departments covering a geographically defined population in the

Stockholm-Uppsala region. Hospital controls were a sample of patients of the same sex and in the same age range as the cases who had a diagnosis of inguinal hernia during the study period at the same surgical departments. Population controls were selected from population registers and matched to the cases by age, sex, and parish. Information on previous occupations and specific occupational exposures was obtained by questionnaire supplemented by telephone interviews. Each case and hospital control received a questionnaire at the time of clinical diagnosis. For each potential case (preliminary diagnosis of pancreatic cancer), a questionnaire was simultaneously sent to the corresponding population control. Subjects who did not return the questionnaire were reminded to do so first by letter and then by telephone. Those who returned a questionnaire were contacted by telephone by a trained interviewer to clarify or complete specific items whenever necessary. Table 1 shows the number of study subjects by case-control status. Of the 120 patients with a final diagnosis of pancreatic cancer, 21 were lost to the study leaving 99 cases (55 men, 44 women). For subjects who were severely ill, it was accepted that the questionnaire was completed by their spouse (see table 1, footnote). The cases were compared separately with each of the two series of controls. The data were stratified by sex, by age in two classes, and by hospital catchment area. The Mantel-Haenszel procedure was used to estimate the relative risks and 90% test based confidence limits were esti-

Table 1 Number of study subjects in the case-control study

	Eligible subjects	Returned questionnaire*	Lost to the study		
			Refused	Died	Not located
Cases	120	99	11	10	0
Hospital controls	179	163	14	1	1
Population controls	162	138	20	0	4

*Includes questionnaires filled in by spouses for 16 cases, two hospital controls, and one population control.

mated using methods based on the Mantel-Haenszel test.¹¹

The retrospective cohort study was based on information from a record linkage between the 1960 census (providing information on age, sex, domicile, and branch of industry for two million employed men aged 20-64 in Sweden) and the Swedish cancer register 1961-79 (providing information on pancreatic cancers diagnosed in that population). Information on the population at risk was obtained from the 1960 census. The observed numbers of cancer in certain occupational groups were compared with the corresponding expected numbers based on the cumulative incidence for all employed men. Stratification was made by age (five year group) and domicile (county). The analysis was based on the standardised morbidity ratio (SMR); 90% confidence limits were assessed according to the method described by Rothman and Boice.¹²

Results

WOOD AND PAPER

Neither the case-control study (table 2) nor the cohort study (table 3) showed an excess risk of pancreatic cancer associated with wood related branches of industry or exposures or with paper manufacturing. In the case-control study only eight subjects (including one case) had an occupational history that included paper manufacturing, but the relative risk

was below unity in the comparison with each control group.

METAL

The findings in the case-control study suggested some excess risk associated with exposure to welding materials (table 2). The cohort study, however, did not show an excess risk among welders (44 cases observed, 44.5 expected). For several other exposures related to metals (including aluminium) the case-control study showed relative risks below or close to unity, although the number of exposed subjects was usually small. In the cohort study SMR values were close to unity for men working in iron and steel works and in iron and steel manufacture (table 3).

PETROLEUM PRODUCTS

In the case-control study there was some evidence of an excess risk associated with a history of employment in the petrochemical industry, although the number of exposed subjects was small: five cases, six hospital controls (RR = 1.9), and 0 population controls (RR = ∞). The cohort study (table 3) showed some excess risk associated with employment in petroleum refineries (SMR = 1.3) and in petrol stations (SMR = 1.6).

OTHER OCCUPATIONAL EXPOSURES

The following three associations were suggested by findings both in the case-control and in the cohort study:

Table 2 Case-control study. Relative risk of pancreatic cancer associated with certain occupational factors, together with 90% confidence limits, as estimated from comparisons with hospital controls and population controls

Exposure	Cases Exposed No	Hospital controls		Population controls	
		Exposed No	Relative risk (90% CL)	Exposed No	Relative risk (90% CL)
Wood powder, sawdust, wood chips	9	22	1.0 (0.5-2.1)	16	0.8 (0.4-1.7)
Surface treatment liquid for wood	6	13	1.4 (0.6-3.3)	9	1.0 (0.4-2.5)
Welding materials	13	27	1.7 (0.9-3.2)	11	2.0 (0.9-4.3)
Soldering materials	12	33	1.1 (0.6-2.1)	13	1.5 (0.7-3.2)
Paint thinners	10	24	1.4 (0.7-2.9)	7	2.5 (1.1-5.9)
Detergents, floor cleaning agents, polish	17	22	1.4 (0.8-2.7)	12	2.2 (1.1-4.2)
Refuse	10	12	1.6 (0.7-3.9)	5	3.7 (1.4-9.7)

Table 3 Cohort study. Standardised morbidity ratio (SMR) for pancreatic cancer in different branches of industry (men), together with 90% confidence limits. Stratification by age and county

Branch of industry	Observed No of cases	Expected No of cases	SMR (90% CL)
Sawmills, carpenters' shops	103	100.0	1.0 (0.9-1.2)
Manufacturing of building joinery	42	42.8	1.0 (0.7-1.3)
Pulp mills	66	71.5	0.9 (0.7-1.1)
Paper & board mills	79	74.6	1.1 (0.9-1.3)
Iron & steel works	122	116.1	1.1 (0.9-1.2)
Iron & steel manufacture	115	128.6	0.9 (0.8-1.0)
Petroleum refineries	10	7.4	1.3 (0.7-2.3)
Petrol stations	20	12.4	1.6 (1.1-2.3)
Painting	95	86.3	1.1 (0.9-1.3)
Paint and varnish factories	13	10.8	1.2 (0.7-1.9)
Washing, ironing, dyeing	16	16.0	1.0 (0.6-1.5)
Floor polishing, window cleaning	8	6.3	1.3 (0.6-2.3)
Refuse disposal works	32	26.4	1.2 (0.9-1.6)

(1) The case-control study indicated some excess risk associated with exposure to paint thinners (table 2), and the cohort study showed SMR values of 1.1 and 1.2, respectively, for employment in painting and in paint and varnish factories (table 3).

(2) An excess risk associated with exposure to detergents, floor cleaning agents, or polish was indicated in the case-control study (table 2). The cohort study showed a SMR value somewhat above unity for men working with floor polishing or window cleaning, but not with washing, ironing, or dyeing (table 3).

(3) In the case-control study there was some excess risk associated with exposure to refuse, and the cohort study showed a SMR value above unity for men employed in refuse disposal plants.

Discussion

When studying the association between occupational factors and pancreatic cancer, it may be difficult to obtain specific information on occupational exposures from the large number of subjects needed for a prospective cohort study. In the studies presented in this paper we have approached this problem in two different ways. In the retrospective cohort study routinely collected information made it possible to study the occurrence of pancreatic cancer in relation to branch of industry for about two million men during a 19 year period. One of the limitations of this approach was that no specific information on chemical or other occupational exposures was available for the individual subjects. Within a single occupational group or branch of industry there may be exposed as well as unexposed subjects, and this would bias the relative risk associated with any specific exposure towards unity. A similar effect would be expected from the lack of information on the number of years spent in the occupation (duration of exposure). In the case-control study it was possible to obtain more specific information on occupational

exposures. Because of the limited number of subjects in that study, however, the number of exposed subjects was often small and it was only possible to study common occupational exposures.

Previous studies have suggested an association between pancreatic cancer and occupational exposure to petroleum products. Pickle and Gottlieb found a raised risk of pancreatic cancer for workers in oil refining⁸ and the findings of Lin and Kessler indicated an association with occupations involving exposure to petrol.¹⁰ We found some support for an association with exposure to petroleum products in the two studies presented here. In the case-control study there was an association with a history of employment in the petrochemical industry, although the number of exposed subjects was small. The cohort study showed SMR values above unity for men employed in petroleum refineries and in petrol stations.

Previous studies indicated raised risks of pancreatic cancer among employees in metal industries and aluminium milling.^{7,9} Our cohort study did not show any excess risk among men working in iron and steel works or in iron and steel manufacture, although there may be some bias towards SMR = 1.0 as mentioned previously. The case-control study suggested an association with exposure to welding materials, but the cohort study did not show an excess risk among welders. No excess risks were found for other exposures related to metals, although the number of exposed subjects in the case-control study was usually small.

Previous studies have also indicated excess risks of pancreatic cancer in wood related occupations^{6,7} and paper manufacturing,⁸ but we found no evidence in support of such associations. For several branches of industry related to wood and paper manufacturing in our cohort study, and for the different exposures related to wood and paper in the case-control study, we found no excess risks of pancreatic cancer.

The findings in our studies suggested some associ-

ations with pancreatic cancer not previously described. The case-control study indicated an association with exposure to paint thinners by comparison with each control group, and the cohort study showed SMR values above unity for men working as painters and in paint and varnish factories. An association with pancreatic cancer was indicated for occupational exposure to detergents, floor cleaning agents, or polish in the case-control study, and for work with floor polishing or window cleaning in the cohort study. The case-control study indicated an excess risk associated with exposure to refuse in the comparison with each control group, and the cohort study showed a SMR above unity for men working in refuse disposal plants. The SMR values in the cohort study were usually rather close to unity, but may be somewhat biased towards unity as mentioned previously. These exposures may be worth considering in future studies, together with occupational exposure to petroleum products.

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