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Mortality and cancer incidence among Swedish paint industry workers with long-term exposure to organic solvents

by Ingvar Lundberg, MD¹

LUNDBERG I. Mortality and cancer incidence among Swedish paint industry workers with long-term exposure to organic solvents. *Scand J Work Environ Health* 12 (1986) 108—113. Cause-specific mortality was studied in a cohort of 416 men who had worked for at least five years in the Swedish paint manufacturing industry during the period 1955—1975. The calculations of expected numbers were based on national, male, calendar-year, and cause-specific death rates for the period 1961—1981. Ninety-six paint industry workers had died, whereas 110 deaths were expected. Three workers had died from multiple myeloma (0.6 expected), and the excess might be related to solvent exposure. Three cleaners had died from infectious urinary tract disease, in comparison to 0.2 deaths expected from all genitourinary diseases, in this small and very heavily exposed group. This association might possibly indicate a modifying effect on the prognosis of urinary tract morbidity from solvents.

Key terms: cohort study, genitourinary disease, multiple myeloma, xylene.

Long-term exposure to organic solvents has been associated with effects on the central nervous system and the skin. Furthermore increased risks of glomerulonephritis and tumors have been suggested. (See reference 6 for a recent review.)

In the late 1970s air measurements of solvents and cross-sectional studies of the health of Swedish paint industry workers were performed. The measurements showed high solvent concentrations in the air in all parts of the factories, xylene usually being the main component in the solvent mixture. Workers engaged in the manual cleaning of paint mixing equipment with solvents, "cleaners", were often exposed to extremely high concentrations (2, 24). The health studies demonstrated impairments on psychometric tests, most pronounced among the cleaners (4), and a tendency towards an increased urinary excretion of albumin, erythrocytes, and leukocytes/renal tubular cells (5). There were no increases in sister chromatid exchanges or chromosome aberrations in peripheral lymphocytes (12) and no signs of liver damage (15).

A cohort study on mortality and cancer incidence is now reported; it complements the comprehensive study of Swedish paint industry workers.

Material and methods

Exposure

Knowledge about the historical occupational exposure in the Swedish paint industry before 1950 is limited. During the 1930s heavy naphthas, as well as toluene and benzene, seem to have been the most commonly used solvents, and the exposure to these compounds was presumably high. During the Second World War and in the immediate postwar period a number of substitutes like sulfate and charcoal terpentine, decaline, tetraline, etc, were used instead of the ordinary chemicals, as the access to aromatic hydrocarbons was limited.

The exposure conditions during the period from 1950 until today have been evaluated through interviews with authoritative representatives of the trade. The most commonly used solvents have been xylene, toluene, white spirit, ethanol, butanol, ethyl acetate, and butyl acetate. The exposure to agents other than solvents, eg, pigments, binders, additives, etc, has generally been limited to the job of charging raw materials.

A crude estimation of the average 8-h exposure for the most common solvents during different periods in all the plants investigated was based on air concentration measurements from 1975 (25) and 1978 (2) and information on work practices, ventilation, etc, from the interviews (table 1). The estimations have been expressed as hygienic effects² based on current Swedish hygienic standards.

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² Hygienic effect is defined as the sum of the fractions of the respective hygienic standards that the exposure to each solvent represents.

Before the late 1960s the paint manufacturing process was largely manual, and the workers were in close contact with the paints. Local exhaust ventilation was practically nonexistent, and work with open holders and at rolling mills was common. After the middle of the 1960s gradual improvements in the work environment have led to pronounced decreases in exposure. See table 1. During the whole period since 1950 xylene and toluene have constituted the major part of the air exposure. The solvent exposure in different factories and the different tasks in the factories were considered to be similar, with the exception of cleaning. The cleaners were very heavily exposed. Hygienic effects corresponding to 5–10 still occurred for them frequently in the late 1970s (2).

Subjects

Nine paint manufacturing companies, located in southern Sweden, provided lists of all their employees who had worked for more than five years in a solvent-exposed environment during the years 1955 to 1975. From 1955 on the company files were stated to be complete. A large number of the workers had worked with several different tasks during their employment, and their individual work histories could not be obtained. However, cohort members who had worked as cleaners for at least two years were identified.

The cohort contained only a few women and was therefore restricted to men. In 1982, 416 men were identified through the national insurance files or parish books as either dead or alive, and they have been followed from 1961 to 1981 for causes of death and from 1961 to 1980 for cases of cancer in the Swedish cancer register. Five more men belonged to the cohort but were lost to follow-up and excluded. The distribution of the cohort members into five-year periods of beginning of employment is shown in table 2. About 30 % of the workers were employed in the paint industry before 1950.

The average exposure during the different periods from 1950 to 1981 (table 1) were multiplied by the length of employment (in years) of the individual worker during the same period. Thus each worker was assigned a number of "hygienic standard years." By dichotomization at the exposure median of 25 hygienic standard years, two subcohorts with "lower" and "higher" exposure were formed. Those cohort members who had worked as cleaners for a minimum of two years were included in these calculations, but they were also treated as a separate exposure group since they presumably had been exposed to very high solvent air concentrations during their period as cleaners. The exposure before 1950 was considered impossible to quantify and could not contribute to the exposure index for the individual worker. However, only eight workers employed before 1950 were referred to the lower exposure category, and therefore this category reflects the conditions in the paint industry after 1950,

Table 1. Average solvent exposure in the paint industry as the hygienic effects during different time periods.

Year	Hygienic effect ^a
1950–1969	2
1970–1974	1.5
1975–1979	0.7
1980–	0.3

^a Hygienic effect is defined as the sum of the fractions of the respective hygienic standards that the exposure to each solvent represents.

Table 2. Distribution of the cohort members according to start of employment.

Year	Number	Cumulative frequency (%)
—1929	5	1
1930–1934	16	5
1935–1939	23	11
1940–1944	30	18
1945–1949	46	29
1950–1954	60	43
1955–1959	73	61
1960–1964	82	81
1965–1970	81	100

while the higher exposure category also, to a significant extent, reflects earlier conditions.

Methods

The expected numbers of deaths and cancers were calculated by multiplying the person-years of observation within five-year age categories during the respective calendar years of the study period by the cause-, sex-, and age-specific national death and cancer incidence rates and by summarizing the fractional contributions for the respective cohorts. In the calculations the computer system EPILIN (Epidemiology in Linköping) at Linköping University, which also calculates 95 % confidence limits for the quotient between observed and expected numbers, has been used (3). The calculation of p-values was based on the Poisson distribution, and the significance level was set at $p=0.05$.

Copies of the death certificates were obtained from the National Bureau of Statistics. The official main cause of death was accepted in all cases except three, where misclassifications had occurred. The correct classification was checked with the National Bureau of Statistics in these cases.

Results

Ninety-six paint industry workers had died during the follow-up period in comparison to the 110 expected (table 3). The lower than expected mortality was primarily caused by a deficit in cardiovascular diseases. Three deaths were caused by multiple myeloma ver-

Table 3. Observed and expected number of deaths among Swedish paint industry workers with at least five years of employment between 1955 and 1975 and no further requirement concerning time between first exposure and observation. Between 1961 and 1981, 6 519 person-years were observed.

Cause of death and ICD ^a number	Observed	Expected	Observed: expected	95 % confidence limits
All causes, 1—999	96	109.7	0.88	0.70—1.06
Tumors, all sites, 140—209	22	26.1	0.84	0.52—1.27
Lung, 162	3	4.8	0.63	0.12—1.84
Lymphatic and hematopoietic tissues, 200—207	5	2.4	2.12	0.68—4.96
Multiple myeloma, 203	3	0.6	5.49	1.13—16.06
Leukemias, 204—207	1	0.9	1.07	0.02—5.95
Diseases of the circulatory system, 390—458	46	56.6	0.81	0.59—1.08
Ischemic heart disease, 410—414	34	40.7	0.83	0.57—1.16
Cerebrovascular disease, 430—438	3	9.1	0.33	0.06—0.96
Diseases of the respiratory system, 460—519	8	5.1	1.56	0.67—3.06
Chronic obstructive lung disease, 490—493	3	2.2	1.38	0.28—4.02
Diseases of the digestive system, 520—577	4	4.7	0.86	0.23—2.20
Cirrhosis of the liver, 571	4	1.7	2.42	0.65—6.18
Diseases of the genitourinary system, 580—607	5	1.9	2.70	0.87—6.29
Accidental deaths, 800—999	9	8.0	1.12	0.51—2.13

^a International Classification of Diseases, eighth revision.

Table 4. Observed and expected number of deaths in the two subcohorts with less than 25 “hygienic standard years” (N = 208) or 25 “hygienic standard years” or more (N = 208) of exposure. (1 = paint industry workers apart from cleaners, 2 = cleaners)

Cause of death and ICD ^a number	Lower exposure				Higher exposure			
	1		2		1		2	
	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected
All causes, 1—999	38	34.1	5	6.5	49	63.6	4	5.5
Tumors, all sites, 140—209	8	7.9	1	1.6	12	15.4	1	1.3
Lymphatic and hematopoietic tissues, 200—207	2	0.7	—	0.1	3	1.4	—	0.1
Multiple myeloma, 203	—	0.2	—	0.0	3	0.3	—	0.0
Diseases of the circulation system, 390—458	15	17.5	2	3.5	28	32.7	1	3.0
Diseases of the respiratory system, 460—519	4	1.6	—	0.3	4	2.9	—	0.3
Cirrhosis of the liver, 571	4	0.6	—	0.1	—	1.0	—	0.1
Diseases of the genitourinary system, 580—607	2	0.6	2	0.1	—	1.1	1	0.1
Accidental deaths, 800—999	4	2.8	—	0.3	5	4.6	—	0.3

^a International Classification of Diseases, eighth revision.

Table 5. Data on the cases of multiple myeloma.

Year of birth	Period of employment	Deceased
1901	1951—1966	1966
1901	1925—1968	1969
1911	1952—1976	1978

sus 0.6 expected ($p < 0.05$). There were tendencies towards an increased mortality from diseases of the respiratory and genitourinary systems and from liver cirrhosis.

The mortality in the subcohorts, defined according to exposure level, is shown in table 4. In the subcohort with “lower” exposure there were more deaths than expected, while the opposite was true in the subcohort with “higher” exposure. The three cases of myeloma had occurred among the workers with “higher” exposure, and the four cases of liver cirrhosis among the workers with “lower” exposure. Three deaths from genitourinary disease had occurred among the cleaners, extracted from the dichotomized subcohort, versus 0.2 expected. The deaths from respiratory disease were evenly distributed between the subcohorts.

When the subcohorts were analyzed with a requirement for at least 15 years' latency time from the beginning of exposure, all three cases of myeloma remained, as well as the cases of genitourinary disease among the cleaners, but all four cases of liver cirrhosis occurred less than 15 years after the beginning of exposure.

Some details concerning the myeloma cases are given in table 5. All five cases of genitourinary disease in the total cohort were due to infectious diseases, and the hospital records did not suggest that any of them was actually a misdiagnosed case of glomerulonephritis. The three deaths among the cleaners were caused by pyelonephritis, acute pyelitis, and urinary tract infection, respectively, and all occurred after the age of 75 years. The deaths from respiratory disease were due to pneumonia (five cases), asthma (two cases), and chronic bronchitis (one case).

In the cancer register 35 cases were found in comparison to the 39 expected. The five cases of malignancies in the lymphatic and hematopoietic tissues (expected 3.2), including the three cases of multiple myeloma (expected 0.6), had been reported to this register. There was no excess morbidity from any other cancers in either subcohort.

Discussion

Work in the paint industry does not seem to entail a generally increased risk in comparison to expected figures calculated from national mortality statistics. An excess frequency from colorectal cancer, but no other cause of death, was reported in a large cohort study of male workers employed in the paint industry in the United States for at least one year between 1946 and 1976 (18). A subsequent case-referent analysis of the material showed that this single excess risk was hardly due to occupation (17). Exposure conditions were only described briefly.

Excess frequency of myeloma has been reported in several epidemiologic studies investigating the association between different industrial exposures and mortality pattern, and it has been proposed that various physical and chemical agents may induce myeloma through chronic antigenic stimulation or the suppression of immune regulatory function. (See reference 7 for a review.) In occupations for which solvent exposure is common [oil refining (22), alkylbenzene production (8), and the rubber industry (9, 10)] workers have died from myeloma more often than expected. At least five years of employment and 20 years of latency were required for the myelomas to appear in the study from the rubber industry. Excess frequencies of other lymphoproliferative neoplasms, ie, lymphatic leukemia and lymphomas, were simultaneously described in some of these studies (10, 22), but also in other studies of solvent exposure (11, 16, 20, 21, 25). Ben-

zene has been suggested as a causative agent for myeloma in some of the studies already cited, as well as in some case reports (1, 23). Benzene exposure is believed to have been low in the paint industry since its use was prohibited already in the beginning of the 1950s, but it appeared as an impurity in other solvents until the beginning of the 1970s.

There are no data in the literature to support an association between infectious diseases of the genitourinary tract and solvent exposure. However, as a rather pronounced excess mortality from genitourinary disease appeared among the cleaners, the possible association with exposure should be further investigated. The slight effect on the kidneys found among solvent-exposed workers (5) might possibly make the kidneys and the urinary tract more susceptible to infections or impair the prognosis of infectious kidney and urinary tract disease.

Paint industry workers, especially those charging raw materials, may be exposed to many vapors and dusts apart from solvents, and their occupational exposure may contain agents that could affect the respiratory tract. Excess deaths due to chronic obstructive lung disease have been reported among painters (11). However, there was only a slight increase in deaths due to respiratory diseases, mainly pneumonia, in our cohort. Further follow-up is warranted to elucidate the possible association between occupational exposure in the Swedish paint industries and respiratory disease.

The expected number of deaths in this study was calculated from the national average mortality rates. The total population contains groups with significantly higher mortality than workers with long-term employment in industry, eg, the unemployed, people who have never worked or left their work early due to disease or handicap, etc. In cohorts of active workers, observed numbers of death therefore often fall short of expected numbers calculated from national averages (14). This pattern is clearly visible in the "higher" exposure category in our cohort. The average employment time in it was about 27 years, and the observed: expected ratio for all mortality was 0.77. In the lower exposure category, with a mean employment time of about 10 years, the observed mortality was higher than the expected. The excess mortality was to a substantial extent caused by excesses from liver cirrhosis and accidental deaths. This finding suggests that workers with a high alcohol consumption have been employed in the paint industry to an unusual extent. Indications of alcohol-related hypermortality have been found among short-term employees in other studies (19).

In a cross-sectional study the serum activities of liver enzymes were not raised, even among very heavily exposed paint industry workers, and selection of workers away from a solvent-exposed environment had not occurred due to signs of liver damage (15). Deaths from liver cirrhosis appeared only in the "lower" exposure category and within less than 15 years from the beginning of exposure. As liver cirrhosis due to alcohol

consumption usually becomes evident only after 20–30 years of excessive drinking, a simple association between the occupational exposure and the cirrhoses seems less likely. However, potential synergistic effects between solvents and alcohol may have contributed to the excess of liver cirrhosis.

Regional differences might bias comparisons with average national statistics. However, the studied paint industries were located both in larger cities and in smaller communities, and from this aspect the comparison with the national statistics should be adequate. Furthermore, the myeloma cases had occurred in regions where the total myeloma incidence was close to the national average.

A series of calculations was performed with different subcohorts defined according to different durations of employment and follow-up subperiods, but the results are not reported as they, in general, do not expand the information. However, the reverse “dose-response” relationship for total mortality that appeared in the total cohort was not found among workers who had terminated their employment before 1970.

Workers employed long term in the Swedish paint industry did not experience any increased risk concerning overall mortality or overall cancer incidence. However, three cases of multiple myeloma versus 0.6 expected were found, and among the heavily exposed cleaners there was an increased mortality from infectious genitourinary disease. These possible associations should be investigated in further follow-up of this cohort, as well as in other studies of solvent-exposed workers.

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