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MULTIPLE MYELOMA AND DIESEL AND OTHER OCCUPATIONAL EXPOSURES IN SWEDISH CONSTRUCTION WORKERS

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We examined the relationships between occupational exposures and the risk of multiple myeloma among male construction workers in Sweden. A total of 446 myeloma subjects were identified among 365,424 male workers followed from 1971 to 1999. Occupational exposure was assessed using a semiquantitative job-exposure matrix, based on a survey carried out by the Construction Industry's Organization for Working Environment, Occupational Safety and Health in Sweden. Rate ratios (RRs) in the exposed groups relative to the unexposed groups were estimated by Poisson regression. We found an increased risk (RR = 1.3, 95% CI 1.04–1.71) among construction workers exposed to diesel exhaust. Adjustment for other occupational exposures did not change this estimate (RR = 1.3, 95% CI 1.00–1.77). However, there was no monotonic increase in risk with estimated level of exposure (RR for low = 1.4, moderate = 1.1, high = 1.4). There was no evidence of increased risk associated with the other occupational exposures among these construction workers, including asbestos, asphalt, cement dust, metal dust, mineral wool, organic solvents, stone dust and wood dust. Occupational exposure to diesel exhaust in the Swedish construction industry may present a small risk of multiple myeloma, but lack of an exposure–response trend tempers our ability to draw clear conclusions.

Key words: *construction industry; diesel exhaust; multiple myeloma; occupational exposure; Sweden*

The incidence of multiple myeloma has gradually increased in many countries, and incidence rates show considerable international variation.[1] Sweden has one of the highest incidence rates of multiple myeloma in both men and women, with age-adjusted rates of 7.4/100,000 and 5.1/100,000 in 1992, respectively.[2] Incidence rates for multiple myeloma in Sweden are expected to increase about 1.0% per year for the next several years.[3] A survey in Sweden concluded that rising rates could not be entirely explained by diagnostic improvements.[4]

The role of occupational exposures in the risk of myeloma is not clear. A number of reports have linked multiple myeloma to occupations including farming, petroleum refining, rubber manufacturing and wood production and to specific occupational agents such as asbestos, pesticides, solvents, engine exhaust and metals.[5] However, there have been limited numbers of epidemiologic studies among construction workers.[6,7]

The construction industry is one of the largest industries in Sweden, and workers have potential exposure to a number of hazardous substances, such as asbestos, asphalt, dust and organic solvents. Exposure to diesel exhaust is also possible through the operation of heavy equipment.[8] To provide additional information on risk of multiple myeloma for exposures in the construction industry, we took advantage of a large data set in this industry with detailed occupational and other information on possible risk factors for cancer.

MATERIAL AND METHODS

This cohort has been previously described in detail.[9,10] Briefly, the Swedish construction industry set up a national health service for workers in the late 1960s, the Construction Industry's Organization for Working Environment, Occupational Safety and Health (in Sweden known as *Bygghälsan*). Although the program was voluntary, approximately 80% of eligible workers participated at least once. The cohort includes 365,424 male employees who entered the program during the period 1971–1993. Information on job title, specific exposures, smoking history, height and weight was obtained. The information has been computerized, and individual workers have been linked to the Swedish National Cancer Registry through 1999 to identify incident cases of multiple myeloma and other cancers. Each worker was followed from date of enrollment through 31 December 1999, with a loss of follow-up of <0.1%. We examined the incidence of multiple myeloma (ICD-7 203). Only first primary cancers were included.

A JEM was developed for selected exposures, *i.e.,* diesel exhaust, asbestos, organic solvents, metal dust, asphalt, wood dust, stone dust, mineral wool and cement dust, focusing on exposures occurring during the mid-1970s. Assessments were made for over 300 occupational job codes for the industry. The exposure assessment was based on a survey of occupational exposures carried out by the Construction Industry's Organization for Working Environment, Occupational Safety and Health,[11] from 1971 through 1976. Several chemical exposures were assessed, along with other occupational factors and hazards by a group of occupational hygienists and physicians. Each exposure was graded on a relative scale of 0–5. Although, level 3 corresponded to the threshold limit value for that exposure, no specific quantitative meaning was assigned to the other grades.

Nitric oxide served as a marker for diesel exhaust. For diesel exhaust, the highest grading was 2, which corresponded to a level below the Swedish threshold limit for nitric oxide of 2 ppm (3.5 mg/m^3).[12] Few occupations were considered to have diesel exhaust exposure in the original survey. Subsequently, an exposure grade of 0.5 was added to the scale for diesel exhaust, to identify the relatively low-exposure occupations. Drivers (including machine operators), asphalt workers, earthmoving workers, mountain workers and some repairers and concrete workers were classified as exposed to diesel exhaust in this cohort (Appendix).

Person-years for each cohort member were computed from the date of first entry into the cohort to the date of a multiple myeloma diagnosis, death, emigration or 31 December 1999, whichever occurred first. Poisson regression analysis using the EPICURE

Abbreviations: BMI, body mass index; CI, confidence interval; JEM, job-exposure matrix; PAH, polycyclic aromatic hydrocarbon; RR, rate ratio; SES, socioeconomic status; SIR, standardized incidence ratio; SMR, standardized mortality ratio.

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program was conducted to examine internal exposure–response relations and to explore the effect of potential confounding factors.[13] RRs were adjusted for age (≤49, 50–59, 60–69, ≥70), BMI (≤24.9, 25.0–29.9, ≥30.0) and other occupational exposures. We first calculated relative risks by ever/never categories and then carried out exposure–response analyses using the low, moderate and high categories of exposure according to the JEM. For diesel, this corresponded to 0 = never, 0.5 = low, 1 = moderate and 2 = high.

RESULTS

The vital status of subjects is presented in Table I. The cohort contributed 7,062,984 person-years of observation from 1971 to 1999, yielding a total of 446 primary incident multiple myeloma cases. In the entire cohort, 1.8% of workers had emigrated.

Basic characteristics of the subjects and their risks are presented in Table II. Risks of multiple myeloma increased sharply with age. Age-adjusted RRs were not associated with smoking status or SES, whereas the RR for multiple myeloma was significantly decreased among obese workers (BMI ≥30; RR = 0.6, 95% CI 0.4–0.9).

RRs for multiple myeloma by specific occupational exposures are presented in Table III. The age- and BMI-adjusted RR was significantly increased for diesel-exposed workers (RR = 1.3, 95% CI 1.04–1.71). Further adjustment for other occupational exposures did not change the risk (RR = 1.3, 95% CI 1.00–1.77). Multiple myeloma was not associated with exposures to asbestos, asphalt, cement dust, metal dust, mineral wool, organic solvents, stone dust or wood dust.

RRs for multiple myeloma by level of diesel exposure are presented in Table IV. There was no evidence of an exposure–response relationship. Indeed, RRs for multiple myeloma at low (RR = 1.4, 95% CI 0.99–1.92) and high (RR = 1.4, 95% CI 0.77–2.59) levels of exposure were equivalent. The similar analyses for other exposures are not presented because they were not noteworthy.

RRs for multiple myeloma among drivers with and without diesel exposure are shown in Table V. Although all drivers/diesel categories had slightly increased relative risks, the RR for nondrivers with exposure to diesel exhaust was slightly larger (RR = 1.4, 95% CI 0.99–1.86) than that of drivers with diesel exposure.

DISCUSSION

There was a small but significantly increased incidence of multiple myeloma among Swedish construction workers exposed to diesel exhaust. Relative risks, however, did not rise with increasing level of exposure.

Our findings are consistent with several previous epidemiologic studies that have reported an association between exposure to diesel exhaust and risk of multiple myeloma. An association was first suggested in a Swedish case-referent study.[14] The magnitude of risk that we observed (RR = 1.3) is similar to that found in several other case-control studies of multiple myeloma, diesel exposure and employment in the construction industry.[15–20] Results from cohort studies of diesel exhaust, however, have been equivocal. In an earlier follow-up of this cohort, drivers had a higher SIR (2.7) and SMR (3.7) for multiple myeloma.[7] However, these results were based on a small number of cases with a follow-up period until 1992. In a Danish cohort study of truck drivers, Hansen[21] reported an increased risk of multiple myeloma among those exposed to diesel exhaust (SMR = 4.4). Analysis of data from the Swedish Cancer–Environment Registry did not show an increased risk of multiple myeloma with diesel exposure (SIR = 1.0)[22] or with occupation in the construction industry (SIR = 1.1).[6] In the American Cancer Society Prospective Study, a small, nonsignificant association between multiple myeloma and diesel exhaust exposure was found based on 14 multiple myeloma cases (cohort study RR = 1.2,[23] nested case-control study OR = 1.4[20]).

Consistent with earlier reports, we saw no evidence of an exposure–response relationship between multiple myeloma and diesel exhaust. The absence of an exposure response could indicate that diesel exposure is unrelated to the development of myeloma. The lack of exposure–response relationship could also be due to misclassification of exposure. Either nondifferential[24] or differential[25] misclassification could diminish an exposure–response pattern. It is relatively easy to mute an exposure–response gradient when the relative risks in the ever exposed are small.

We found the largest RR among diesel-exposed nondrivers. This reflects the increased risk among nondrivers, such as asphalt, transport and assistant workers, who had higher exposure to diesel exhaust according to the JEM (Appendix). Drivers with exposure to diesel exhaust had an increased RR but so did drivers who were not exposed to diesel exhaust. This pattern among drivers with and without exposure to diesel exhaust does not make a strong case for an association between multiple myeloma and diesel exposure and indicates that exposures other than diesel may put drivers at some small risk.

Diesel exhaust emissions are a mixture of gases and particulates, including carbon monoxide, oxides of nitrogen and sulfur and particulates containing traces of nitro-PAHs. In 1989, the IARC classified exposure to diesel exhaust as probably carcinogenic to humans based on sufficient evidence of carcinogenicity in experimental animals and limited evidence of carcinogenicity in humans.[26] Although the molecular basis of diesel carcinogenicity is unclear, exhaust emission from diesel engines contains nitro-PAHs, which have been demonstrated to be mutagenic and carcinogenic in *in vitro* tests.[26–28]

Other occupational exposures, including asbestos, metal dust, organic solvents and wood dust, have been identified as possible risk factors for multiple myeloma.[14,29–31] These exposures were not associated with multiple myeloma risk in our cohort.

Our finding of a decreased risk for BMI of ≥30 is not consistent with the results of the 2 previous studies of BMI and multiple myeloma.[32,33] These studies suggested that BMI was positively associated with risk of multiple myeloma; however, they were not consistent across race and sex groups.[32] We observed no association with smoking and risk, which is consistent with most previous epidemiologic studies of multiple myeloma.[5,34–37] Although we found no association between SES and multiple myeloma, this relationship remains possible.[38–42] Since all subjects in this analysis were Swedish construction workers, the SES range for this cohort may be too narrow to observe an effect.

The main strength of our study is the availability of information on potential confounders, including BMI, smoking, SES and other occupational exposures. We lacked information on alcohol consumption, but this factor does not appear to be associated with multiple myeloma and is not likely to confound risk estimates.[36,43] The large size of the cohort and the availability of cancer incidence data are additional strengths. Exposure assessment based on a JEM developed for this cohort is another advantage compared to those previous studies where exposure was self-reported. The previously reported results on asbestos exposure and lung cancer among the Swedish construction workers based on this JEM indicated a better ability to discriminate between high- and low-risk groups than self-reported exposure.[44]

TABLE I – NUMBER OF SUBJECTS, PERSON-YEARS AND MULTIPLE MYELOMA CASES BY VITAL STATUS

Vital status	Number of subjects (%)	Person-years of follow-up (%)	Number of incident cases (%)
Alive	306,871 (84.0)	6,186,292 (87.6)	93 (20.9)
Dead	51,875 (14.2)	816,879 (11.6)	353 (79.1)
Emigrated	6,678 (1.8)	59,813 (0.8)	0 (0.0)
Total	365,424 (100)	7,062,984 (100)	446 (100)

TABLE II – RRs FOR MULTIPLE MYELOMA ACCORDING TO AGE, SMOKING, SES AND BMI

Characteristics	Number of cases	RR unadjusted	95% CI	RR age-adjusted	95% CI
Age (years)					
≤ 49	37	1.0	Ref[1]	—	—
50–59	84	8.1	5.48–11.88	—	—
60–69	162	22.0	15.38–31.41	—	—
≥ 70	163	41.0	28.69–58.59	—	—
Smoking					
Nonsmoker	135	1.0	Ref	1.0	Ref
Ex-smoker	91	1.7	1.28–2.18	1.1	0.85–1.44
Current	170	1.2	0.98–1.54	1.0	0.81–1.27
SES					
White collar	16	1.0	Ref	1.0	Ref
Blue collar	430	0.9	0.53–1.45	1.1	0.66–1.79
BMI (kg/m^2)					
≤ 24.9	231	1.0	Ref	1.0	Ref
25.0–29.9	195	1.8	1.51–2.20	1.0	0.79–1.17
≥ 30.0	19	1.2	0.76–1.94	0.6	0.36–0.92

[1]Ref, reference category.

TABLE III – RRs FOR MULTIPLE MYELOMA ACCORDING TO OCCUPATIONAL EXPOSURES

Occupational exposures	Number of cases	RR[1]	95% CI	RR[2]	95% CI
Asbestos					
Never	384	1.0	Ref[3]	1.0	Ref
Ever	12	0.8	0.42–1.34	0.9	0.37–1.94
Asphalt					
Never	390	1.0	Ref	1.0	Ref
Ever	6	1.0	0.44–2.24	0.8	0.35–1.85
Cement dust					
Never	347	1.0	Ref	1.0	Ref
Ever	49	1.0	0.76–1.38	1.0	0.68–1.37
Diesel exhaust					
Never	317	1.0	Ref	1.0	Ref
Ever	79	1.3	1.04–1.71	1.3	1.00–1.77
Metal dust					
Never	367	1.0	Ref	1.0	Ref
Ever	29	0.9	0.60–1.27	0.9	0.58–1.37
Mineral wool					
Never	374	1.0	Ref	1.0	Ref
Ever	22	0.8	0.53–1.24	1.0	0.51–1.77
Organic solvents					
Never	355	1.0	Ref	1.0	Ref
Ever	41	1.1	0.80–1.52	1.2	0.83–1.62
Stone dust					
Never	298	1.0	Ref	1.0	Ref
Ever	98	1.1	0.84–1.33	1.0	0.74–1.39
Wood dust					
Never	376	1.0	Ref	1.0	Ref
Ever	20	0.8	0.49–1.20	0.8	0.49–1.23

[1]Adjusted for age and BMI. –[2]Adjusted for age, BMI and other occupational co-exposures (ever/never exposed to asbestos, asphalt, cement dust, diesel exhaust, metal dust, mineral wool, organic solvents, stone dust, wood dust). –[3]Ref, reference category.

Although the JEM was developed for our study in particular, some nondifferential misclassification might have occurred. This would bias the results toward the null and might explain some of our negative findings.

Other limitations of our study include the lack of information on duration of exposure and the date of first exposure. Consequently, we were unable to analyze risk by duration of diesel exhaust exposure or latency. A high turnover rate within an industry may lead to short duration of exposure and a low level of cumulative exposure, which would make finding an association, if it existed, difficult. The Swedish construction industry, however, is known to have a stable work force.[10] A second limitation was the low-level diesel exhaust exposure to which workers in the cohort were exposed, making it difficult to discern an effect.

TABLE IV – RRs FOR MULTIPLE MYELOMA BY LEVELS OF DIESEL EXPOSURE

Diesel exposure	Number of cases	RR[1]	95% CI	RR[2]	95% CI
Never	317	1.0	Ref[3]	1.0	Ref
Low	52	1.4	1.05–1.88	1.4	0.99–1.92
Moderate	10	1.1	0.57–2.01	1.1	0.56–2.04
High	17	1.3	0.81–2.16	1.4	0.77–2.59

[1]Adjusted for age and BMI. –[2]Adjusted for age, BMI and other occupational co-exposures (ever/never exposed to asbestos, asphalt, cement dust, diesel exhaust, metal dust, mineral wool, organic solvents, stone dust, wood dust). –[3]Ref, reference category.

TABLE V – RRs OF MULTIPLE MYELOMA ASSOCIATED WITH EMPLOYMENT AS A DRIVER AND POTENTIAL DIESEL EXPOSURE

Diesel exposure	Driver	Number of cases	RR[1]	95% CI	RR[2]	95% CI
No	No	312	1.0	Ref[3]	1.0	Ref
No	Yes	5	1.2	0.49–2.88	1.2	0.48–2.82
Yes	No	57	1.4	1.02–1.79	1.4	0.99–1.86
Yes	Yes	22	1.3	0.83–1.98	1.2	0.77–2.00

[1]Adjusted for age and BMI. –[2]Adjusted for age, BMI and other occupational co-exposures (ever/never exposed to asbestos, asphalt, cement dust, diesel exhaust, metal dust, mineral wool, organic solvents, stone dust, wood dust). –[3]Ref, reference category.

In summary, we saw a small increase in the risk of multiple myeloma from potential exposure to diesel exhaust but no association with other substances. The lack of a clear exposure–response gradient makes it difficult, however, to draw clear conclusions. Future studies with diesel exhaust exposure information by level of intensity, duration and latency are needed to clarify the role of diesel exhaust in multiple myeloma carcinogenesis.

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APPENDIX – JOB DESCRIPTIONS OF DIESEL-EXPOSED WORKERS WITH CASES OF MULTIPLE MYELOMA

Diesel exposure levels	Job descriptions	Number of subjects	Number of incident cases
2	Asphalt work	1,756	3
2	Transport and store work, transport of liquid floors (concrete works)	4,013	14
1	Machine operators (earthmoving)[1]	612	2
1	Machine operators (excavating)[1]	562	2
1	Crushing mill work	177	1
1	Stone crusher work	83	1
1	Repair work (of machines and equipment)	2,152	4
0.5	Operation and maintenance of asphalt works	705	2
0.5	Piling (including tongue-and-groove, concrete works)	138	2
0.5	Car driving[1]	3,652	11
0.5	Earthmoving (embankments)	919	4
0.5	Reception of filling material, control work (earthmoving works)	735	2
0.5	Shaft, pipe and foundation laying (earthmoving works)	8,053	15
0.5	Machine operators (loading machine operating)[1]	1,312	3
0.5	Machine operators (road grader operating)[1]	650	3
0.5	Machine operators (tractor, dumper and forklift truck operating)[1]	1,174	1
0.5	Blasting work (including drilling, mountain works)	2,287	8
0.5	Cleaning work (mountain works)	23	1
Total		29,003	79

[1]Classified as a driver.