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Minnesota Highway Maintenance Worker Study: Cancer Mortality

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Highway maintenance workers (HMWs) have been exposed to a broad range of potentially toxic substances, including diesel fuels and exhaust, asphalts and tars, herbicides, gasoline, polynuclear aromatic hydrocarbons, benzene, and lead. The number of current and former state, county, and municipal HMWs in the United States exceeds 500,000, yet the health risks of this occupation had never been studied. To fill this void and to respond to the public perception that Minnesota HMWs were at high risk of developing leukemia, an occupational cohort mortality study was conducted of Minnesota HMWs employed between 1945 and 1984. Leukemia mortality in HMWs with 30–39 years of work (standardized mortality ratio [SMR] = 425; 95% confidence interval [CI] = 171–876) and urologic cancer mortality in HMWs with 40–49 year latency (SMR = 292; CI = 117–602) were significantly elevated. The extent to which these and other findings were directly related to work exposures is unknown. Further investigations to resolve the significance of the risks associated with the HMW occupation are currently underway.

Key words: leukemia, highway maintenance, mortality cohort cancer

INTRODUCTION

A preliminary investigation of a reported excess of leukemia in a small western Minnesota community in 1978 confirmed that six cases of leukemia in males occurred over a 10-year period, while only one case was expected. It was further found that five of the six cases had been employed as state or county highway maintenance workers (HMWs), an uncommon occupation in this population. A small case-control study in 1979–1980 among HMWs with and without leukemia failed to find significant differences with respect to occupational histories, smoking experience, farming activities, or other potential risk factors.

In 1984, after renewed publicity and speculation arising from worker's com-

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pensation litigation, the Minnesota Department of Health (MDH) determined that a cohort mortality study of HMWs would be necessary to address the potential occupational health risks experienced by HMWs. This conclusion was based on four considerations: 1) no published studies were available on this occupation; 2) the observed leukemia cluster did not establish that highway workers were at increased risk (no other reports of unusual leukemia occurrence in these workers had been received, although it was established that HMWs elsewhere had similar work experiences. More important, unusual clusters of leukemia and other cancers [Caldwell and Heath, 1976; Pike and Henderson, 1980] have frequently been reported throughout the United States, and these clusters can rarely be attributed to specific exposures); 3) review of highway maintenance work indicated that it involved a variety of substances or exposures that are potentially harmful; (these substances include asphalts and tars, diesel fuels and exhausts, gasoline, polynuclear aromatic hydrocarbons [PAH], herbicides, benzene, and lead. Considering the potential for diverse types of exposure, cancer risks other than leukemia needed to be considered in any evaluation of these workers); and 4) the number of current and former HMWs employed at all levels of government in the United States (city, county, and state) exceeded 500,000. Thus, even modest risks could affect a large number of persons.

The cancer mortality experience of Minnesota HMWs reported here is from an occupational cohort mortality study conducted during 1984–1986. Noncancer mortality findings are presented elsewhere [Parker et al., 1988].

METHODS

The methods employed in the Minnesota HMW mortality study have been previously described [Parker et al., 1988]. Briefly, 4,849 men with 1 or more years of experience as a HMW for the Minnesota Department of Transportation (MNDOT) who had worked at least 1 day after January 1, 1945, were eligible for inclusion in the study. The discontinuous work histories were accommodated by detailed abstraction of personnel records that allowed for gaps in employment. Each worker was traced to determine his vital status as of December 31, 1984. If a person died, the cause of death as listed on the death certificate was determined. The vital status of 99.6% of the 4849 eligible workers was determined, and death certificates on 99.9% of the deceased members of the cohort were obtained.

The study spanned five revisions of the International Classification of Diseases (ICD), and the underlying causes of death were coded in the ICD version in effect at the time of death. With the exception of lymphoreticular malignancies, causes of death coded by different ICD revisions were translated into a unique ICD code representing the specificity of ICD5. ICD5 lacked categories for lymphosarcoma and multiple myeloma, and for these malignancies, the ICD6 specificity was used. The translation algorithms were based on coding schemes created by the National Institute of Occupational Safety and Health (NIOSH) [Bender et al., 1987]. Table I contains the ICD9 equivalent codes used to define the cancer causes of death reported in this study.

The white male Minnesota mortality experience was used to calculate the expected number of deaths in the HMW cohort. The comparison population's underlying causes of death that occurred during five ICD revisions (1945–1984) were translated to a common (ICD5) cause of death in the identical manner as the HMW

TABLE I. SMRs for Selected Cancers Among the HMW Cohort, 1945–1984*

Cancer	Observed no. of deaths	Expected no. of deaths	SMR	95% confidence interval
All cancer (140.0–208.9)[a]	274	328.8	83	73–94
Mouth, pharynx (140.0–149.9)	7	8.0	88	35–181
All gastrointestinal (150.0–159.8)	90	109.2	82	66–101
Stomach (151.0–151.9)	23	25.2	91	58–137
Intestines (152.0–153.9)	30	34.9	86	58–123
Rectum (154.0–154.8)	8	12.1	66	28–130
Pancreas (157.0–157.9)	17	19.2	89	52–142
All respiratory (160.0–165.9)	57	82.6	69	52–90
Trachea, bronchus, lung (162.0–162.8)	54	77.9	69	52–90
Male genital (185.0–187.9)	41	39.5	104	75–141
Prostate (185.0–185.9)	39	38.1	100	71–137
Testes (186.0–186.9)	2	0.9	217	26–783
Urinary organs (188.0–189.9)	19	20.7	92	55–144
Kidney (189.0–189.2)	6	9.6	63	23–137
Bladder (188.0–188.9)	12	11.0	109	56–190
Lymphoreticular (200.0–208.9)	34	35.7	95	66–133
Lymphosarcoma (200.0–200.8)	7	6.2	113	45–233
Hodgkin's disease (201.0–201.9)	2	3.4	58	7–209
Leukemia (204.0–208.9)	17	15.9	107	62–171
Multiple myeloma (203.0–203.1)	3	5.7	53	11–155
Other lymphoreticular (202.0–202.9)	5	4.5	110	36–257
Other				
Melanoma (172.0–172.9)	0	2.9	0	—
CNS (191.0–192.9)	6	9.2	66	24–144

*All cause SMR = 91.
[a]ICD 9th revision equivalents.

cohort. Since there are several important urban/rural differences in cancer mortality including leukemia [Wen et al., 1983; Gardner, 1986], both the HMW cohort and the entire Minnesota comparison population were also divided into urban and rural subpopulations.

After the cohort and comparison populations were assembled, standardized mortality ratios (SMR) using the person-years at risk algorithm described by Hill [1972] and previously implemented by Monson [1974] and others [Wen et al., 1983; Waxweiler et al., 1983] were calculated. The patterns of mortality were calculated by combinations of the following variables: age at death; calendar year of death; age started work; year started work; years worked; and latency. Latency represented the length of time since a person first started work (i.e., first date as a HMW) until death, loss to follow-up, or termination of the study. Confidence intervals (95% and 99%) for all SMRs were also calculated [Bailar and Ederer, 1964].

RESULTS

Based on 1,530 deaths among the 4,849 HMWs during the 40-year follow-up of the cohort, the overall SMR in the HMW cohort was 91 with a 95% confidence interval of 86–96. There were 96,567 years of follow-up, and 1,676 deaths were

TABLE II. SMRs for Urinary Cancers in HMWs With 40–49 Years Latency

Year started	Observed no. of deaths	Expected no. of deaths	SMR	95% confidence interval
1900–1924	0	0.5	0	—
1925–1934	2	1.2	170	21–614
1935–1944	5	0.8	656	212–1,533
Total	7	2.4	292	117–602

expected. Major categories contributing to this deficit were heart disease (SMR = 93), cerebrovascular disease (SMR = 80), and cancer (SMR = 83).

Table I contains the observed number of deaths, expected number of deaths, the SMRs, and 95% confidence intervals for selected cancer deaths compared with other white male Minnesotans of the same age and calendar period of death. There were 274 cancer deaths. The overall SMR for all cancer deaths was 83 ($p < .01$). There was no evidence that the SMR increased with increasing number of years worked or increasing latency. The only decade starting work for which the all cancer SMR was greater than 100 was 1955–1964 with an SMR of 111.

There were seven deaths from cancer of the mouth and pharynx. Men that worked 40 or more years had an SMR of 1,110 ($p < .05$). There were only two deaths in this subgroup, and all of the risk was incurred by men who started work in the years 1900–1924. No increased SMRs were found in men working 40 or more years who started work after 1925.

The overall SMR for all gastrointestinal cancer was 82, with a total of 90 deaths. None of the SMRs for this general category was significantly elevated, and there was no trend with increasing number of years worked. For mortality resulting from intestinal cancer, the picture was very similar. The SMR for all workers was 86, based on 30 deaths, and there was no pattern of an increasing SMR with number of years worked or year started work. Urban workers had a somewhat different profile. Their overall SMR was 139, based on 11 deaths. For urban workers with 40–49 years of latency, there was an SMR of 582 ($p < .05$) based on three deaths. All three deaths were due to colon cancer in workers who had started in 1935–1944.

The HMWs had an SMR of 69 ($p < .05$) for lung and other cancers of the respiratory system. The SMR did not increase with length of work or year started. Decreased respiratory cancer mortality was found for both urban and rural HMWs.

Overall mortality caused by prostate cancer was not elevated (SMR = 100). However, based on 11 deaths, workers starting in 1955–1964 had a significantly elevated SMR of 298 ($p < .01$). The increased prostatic cancer mortality was due to workers starting in 1955–1964 at the age of 40 or older. Curiously, men who started work between 1935 and 1944 at the age of 40 or older had a significantly reduced SMR of 46 ($p < .05$).

The SMR for cancers of the kidney, bladder, and other urinary organs was 92, based on 19 deaths. There were no SMR trends with latency or length of work. However, based on seven deaths, workers with 40–49 years of latency had an SMR of 292 ($p < .05$) (Table II). This result was due primarily to workers who started in 1935–1944 who had an SMR of 656 ($p < .01$). A nonsignificantly elevated SMR of 170 was found for workers who started in 1925–1934. The increased SMR for workers with 40–49 years latency was due to both kidney and bladder cancers. SMRs did not increase with the number of years worked for either kidney or bladder cancer.

TABLE III. SMRs for Leukemia in HMWs With 30–39 Years of Work

Year started	Observed no. of deaths	Expected no. of deaths	SMR	95% Confidence interval
1900–1924	1	0.5	216	6–1,200
1935–1934	4	0.8	475	129–1,215
1935–1944	2	0.3	731	89–2,639
1945–1954	0	0.1	0	—
Total	7	1.6	425	171–876

Lymphoreticular malignancies include leukemias, lymphomas, Hodgkin's disease, multiple myeloma, and mycosis fungoides. There were 34 deaths in this category, with an overall SMR of 95. Based on nine deaths, there was a significantly elevated SMR of 241 ($p < .05$) for persons with 30–39 years of work experience. There was also a statistically significant ($p < .01$) trend of increasing SMR with an increasing number of years worked.

Deaths due to leukemia were the major contributor to the significant SMR for lymphoreticular malignancies. There were 17 deaths from all leukemias during the 40-year follow-up. The overall SMR was 107, and all the deaths occurred in the last two decades (1965–1974 and 1975–1984). For the first 20 years, 4.7 deaths were expected, and none occurred. Based on seven deaths, HMWs with 30–39 years of work experience had an SMR of 425 ($p < .01$) with contributions to this elevated SMR from the workers that started in 1900–1924, 1925–1934, and 1935–1944 (Table III). No deaths were observed for workers with less than 5 years experience, while 3.3 deaths were expected. Both urban and rural HMWs with 30–39 years of work had a significantly ($p < .05$) increased leukemia mortality.

The elevated leukemia SMR among workers with 30–39 years of work experience did not change if the four leukemia deaths in MNDOT HMWs that were part of the previously reported leukemia cluster were excluded. None of the four previously known cases had worked more than 29 years. The distribution of leukemia deaths by type of leukemia for both the entire cohort and for workers with 30–39 years of experience was similar to the expected distribution based on Minnesota statistics ($p > .1$). The total number of leukemia deaths, as well as the individual subtypes of leukemia, was in excess, with no subtype disproportionately represented. A detailed description of the 17 workers that died of leukemia is given in Table IV.

During cohort tracing, deaths that occurred after December 31, 1984, were occasionally found, and their documentation filed for later updates. Therefore, knowledge of the mortality experience of all workers after 1984 is incomplete. However, two additional leukemia deaths were identified among those known to have died after 1984. One person worked 32 years and started in the period 1945–1954. Another worked 19 years and started in the same time period. Using these data, it was possible, in a conservative manner, to update the leukemia mortality. Estimates of the smallest SMRs for leukemia deaths for workers with 30–39 years of work experience were calculated on the assumption that no other leukemia deaths occurred and that all workers alive on December 31, 1984, were also alive as of December 31, 1986. The true SMRs must be larger since the number of leukemia deaths was at least one and the expected number of deaths was inflated by assuming all workers lived another 2 years. As shown in Table V, it appears that the leukemia risk has not subsided for

TABLE IV. Detailed Description of the Seventeen Leukemia Deaths in Highway Maintenance Worker Cohort (1945–1984)

Leukemia type	Year started	Year ended	Years worked	Date of death	Years latency	Age at death	Included in index report
Chronic lymphocytic	1930	1974	39	1983	53	74	No
Chronic lymphocytic	1922	1959	36	1978	56	80	No
Chronic myelogenous	1939	1975	35	1979	40	66	No
Lymphocytic	1927	1964	33	1966	39	63	No
Lymphocytic	1932	1966	34	1967	35	67	No
Chronic myelogenous	1939	1973	34	1976	37	64	No
Chronic myelogenous	1933	1965	33	1979	46	76	No
Acute lymphocytic	1934	1958	22	1968	34	75	No
Chronic myelogenous	1933	1956	22	1972	39	84	No
Chronic myelogenous	1938	1959	21	1977	39	73	Yes
Chronic lymphocytic	1933	1961	19	1975	42	78	Yes
Acute myelogenous	1963	1975	12	1982	19	72	Yes
Chronic lymphocytic	1953	1965	10	1971	18	60	No
Acute myelogenous	1964	1975	9	1975	11	48	No
Chronic myelogenous	1965	1974	9	1974	9	54	Yes
Chronic myelogenous	1951	1956	5	1970	19	57	No
Acute myelogenous	1960	1965	5	1972	12	76	No

Years worked do not always equal the difference between the year started and year ended work since work records were often discontinuous.

TABLE V. Estimated Minimum Leukemia SMRs for HMWs With 30–39 Years of Experience With Follow-up Through December 1986

Year started	Observed no. of deaths	Expected no. of deaths[a]	SMR	95% confidence interval
1900–1924	1	0.5	216	6–1,200
1925–1934	4	0.8	471	128–1,205
1935–1944	2	0.3	625	76–2,256
1945–1954	1	0.1	909	23–5,050
Total	8	1.8	449	194–884

[a]Assumes all workers alive as of December 31, 1984, were also alive on December 31, 1986.

HMWs with 30–39 years of work.

There were no deaths resulting from melanoma, whereas 2.9 were expected; there were no deaths caused by soft tissue cancers, whereas 1.4 were expected.

DISCUSSION

A significant reduction of mortality for all causes of death in the HMW cohort was not surprising. Highway maintenance work is physically demanding, and those choosing this occupation cannot be considered as representative of the general Minnesota population. The lower overall mortality experience of working populations, compared with the general population, referred to as the "healthy-worker effect," is a common observation in epidemiologic studies that has been widely discussed [Weed, 1986]. Although attributed in part to a selection process in which healthier persons become or remain employed [McMichael, 1976], it has recently

TABLE VI. SMRs for Selected Smoking-Related Causes of Death

Cause of Death	No. of deaths	SMR
Cancer of lung and bronchus	54	69
Chronic bronchitis	7	147
Emphysema	19	94
Chronic obstructive pulmonary disease	30	108
Cancer of mouth and pharynx	7	88
Kidney and bladder cancers	19	92
Total	136	85
Total (excluding lung cancer)	82	101

been postulated that the existence of a healthy-worker effect in employed cohorts may be an artifact of incomplete follow-up and inaccurate ascertainment of vital status [Vena et al., 1987]. In this study, 99.6% of the cohort was successfully traced and 99.9% of the death certificates of the deceased cohort members were obtained. In addition, 432 of the 4,326 members of the cohort submitted to the SSA for follow-up were already known to be dead. The SSA indicated that only four (0.9%) of these 432 were alive. Therefore, it is unlikely that the reduced overall SMR observed in this cohort represented a bias of incomplete follow-up or inaccurate vital status.

The significantly reduced mortality for all cancer was interesting for three reasons. First, factors thought to influence cancer mortality usually do not affect employment before disease onset (i.e., the healthy-worker effect has little impact on cancer mortality) [McMichael, 1976; Carpenter, 1987]. Second, when the SMR for all cancers is significantly reduced, it is usually larger, not smaller, than the SMR for all cause mortality [Monson, 1986]. Third, as seen in Table I, the major contributor to the significantly reduced all-cancer mortality was the signficant reduction in lung cancer. The reduction in lung cancer mortality is strongly suggestive of decreased cigarette smoking in the HMW cohort. This interpretation is inconsistent, however, with the SMRs for other smoking-related causes of death, which were nominal (Table VI) and not indicative of decreased smoking experience.

Exposure to diesel exhaust and tar materials has been associated with an increased risk of lung cancer. The lack of excess lung cancer mortality in the HMW cohort is not inconsistent with their exposures. Garshick et al. [1987] found a marginally increased risk of lung cancer mortality in railroad workers exposed to diesel exhausts. However, those at risk worked in confined operations such as inside a round house. Outside workers that maintained the railroad right-of-way (similar to the work performed by highway maintenance workers) were considered not at risk. Hammond et al. [1976] found elevated lung cancer mortality in long-term roofers. It is likely that these men had been exposed to coal tar pitch as well as asphalt. The amount of carcinogenic PAH in coal tar is several orders of magnitude greater than in asphalt [Wallcave et al., 1971; Darby et al., 1986]. Since highway maintenance work in Minnesota has not employed coal tar products for 50 years, HMW exposure to carcinogenic PAHs of pitch was probably much lower than the roofers' exposure.

There were 17 deaths from leukemia during the 40-year follow-up of this study. The largest elevation was for those workers with 30–39 years of experience (SMR = 425). Surprisingly, the high-risk leukemia mortality profile did not include the workers in the originally reported leukemia cluster which had led, in part, to the

conduct of this study. The leukemia SMR for cohort members with less than 30 years of work, which included all of the HMWs in the original cluster, was 72. Therefore, the cluster may represent the common finding of spatial and temporal clustering of leukemia with no apparent etiology [Caldwell and Heath, 1976].

There have been two PMR studies applicable to transportation workers. Maizlish et al. [1986] studied the proportional mortality from 1,570 death certificates of California Department of Transportation workers. Specific job classifications and duration of work were not available. However, among white males, an overall PMR of 157 was found for all hemolymphatic cancers; workers who died after retiring had a PMR of 227 for these cancers. Milham (personal communication) found a summary leukemia PMR of 113 for HMWs in the state of Washington. These findings are consistent with data from the current study.

The leukemia SMR of 425 in the Minnesota study for workers with 30–39 years of experience was based on seven deaths. The finding of an additional leukemia death in this group after December 31, 1984, adds further support to the association between leukemia mortality and the life-long experience of this cohort. Since this additional death occurred in a worker with 30–39 years of experience, attention to this subgroup is justified and makes this specific finding (SMR = 449) less likely to be due to chance.

Radiation [Court-Brown and Doll, 1965; Bizzozero et al., 1966], therapeutic drugs [Hart, 1964; Cohen and Huang, 1973], and benzene [Aksoy et al., 1962; Infante et al., 1977] are established leukemogens. Possible risk factors for leukemia include smoking [Hammond, 1966; Rogot, 1974; Severson, 1987; Sandler and Collman, 1987], viruses [Gallo, 1985], host factors [Fraumeni, 1969] (particularly inherited abnormalities), and other occupational experiences (e.g., solvents [Checkoway et al., 1984] and farming [Blair and White, 1985; Bender et al., 1988]). Unfortunately, it was not possible in this instance to examine a specific exposure dose-response relationship for leukemia mortality. Air monitoring data and work histories lacked the detail required for such estimates. It seems improbable, however, that most of these factors influenced the leukemia mortality of the cohort. There is no reason to suspect viral infections, radiation, and drug and host factors as leukemia-risk factors specific to the HMWs. Three factors, however, require further discussion: smoking, chemicals, and farming.

The associations between smoking and leukemia have generally been weakly positive. Since most blue collar workers in Minnesota have a higher smoking prevalence than the general Minnesota population, it could be argued that some of the leukemia risk in HMWs is associated with smoking. However, as already described, there was an inconsistent picture with respect to other smoking-related deaths: the HMW cohort lung cancer mortality was significantly reduced (SMR = 69), whereas the SMR for other selected smoking-related causes of death was 101 (Table VI). In addition, the increased leukemia mortality among long-term workers (30–39 years) was independent of age. If smoking per se was a leukemia risk factor in this cohort, then the risk should have increased with age. Although the inferences about smoking history based on the mortality profiles are not clear, these findings make it unlikely that cigarette smoking accounted for the increased leukemia mortality.

Environmental exposures to this cohort remain enigmatic. Several studies have shown an association between rural populations and leukemia [Blair et al., 1980]. For HMWs, the largest SMR for leukemia was 1,603 for urban workers with 30–39 years

of experience, compared with 279 for rural workers. The overall SMR for urban workers was 112, compared with 107 for rural workers. Although it can be hazardous to compare indirect standardizations, it is unlikely that farming, most commonly associated with rural life, was a significant risk factor in the etiology of leukemia deaths in this cohort.

Data have been gathered on *current* exposures to benzene by HMWs. Recent breathing zone exposures have been well below the threshold limit value standards (<1 ppm). However, no data were available on past exposures to benzene. Acute nonlymphocytic leukemias are commonly associated with benzene exposure [Aksoy et al., 1976]. In many cases in the literature, leukemia followed benzene exposure by 15 years. There also have been reports of an association between lymphocytic leukemia and solvent exposure [McMichael et al., 1975]. In the studies reporting an increased risk of chronic lymphocytic leukemia [Checkoway et al., 1984], benzene exposures were low and three other solvents were also suspect: hexane, carbon tetrachloride, and carbon disulfide. A case-control study in Sweden [Flodin et al., 1988] found a statistically significant risk (2.5) for chronic lymphatic leukemia in individuals with outdoor exposure to engine exhaust. This risk was thought to be not associated with benzene exposure. These observations, combined with monitoring data showing little evidence of current benzene exposure, leave in question the possibility of exposure to other leukemogens either on or off the job or the possibility of historical exposure to low levels of benzene.

Oral administration of certain PAHs to rodents can produce leukemias in addition to a variety of other malignancies. Analyses of bulk samples of asphalts, oils, and tack coats currently used by Minnesota HMWs, as well as breathing zone samples, failed to detect pyrene, benzo(a)pyrene or chrysene. However, these and other PAHs have been detected in asphalt fumes under both field and laboratory conditions (Brandt et al., 1985]. Although current exposures to these PAHs may be minimal, they provide no basis for inference about historical exposures to these agents. A bulk sample of the tack coats (MC-70) contained 13,100 ppm of dodecane. No standard has been established, but dodecane has been reported to be a cancer promoter [Bingham and Falk, 1969; Horton and Christian, 1974]. Again, the significance of this finding is unknown since historical exposure cannot be evaluated.

There was increased mortality from cancers of the urinary organs for workers with 40–49 years of latency. Of the 19 deaths from urologic cancers, 12 were due to bladder cancer, six to kidney cancer, and one to urethral cancer. Smoking is an established risk factor for bladder cancer [Morrison and Cole, 1982]. The dye industry has also been implicated in bladder cancer. Benzidene and beta-naphthylamine have been identified as potent bladder carcinogens. In addition, associations between several other trades and bladder cancer have been found. These trades include rubber, leather, and textiles. It is typical to have long induction periods for bladder cancer, especially with weaker cancer-causing agents. With the exception of smoking and possibly obesity [McLaughlin et al., 1984; Goodman et al., 1986], other risk factors for kidney cancer, including gasoline exposure, are very speculative [Domiano et al., 1985] and an occupational etiology cannot be ruled out.

Only a few occupational studies of prostatic cancer have been reported [Armstrong and Kazantzis, 1985; Ross et al., 1987], and their findings are equivocal. Prostatic cancer may be related to sexual activity, dietary factors, race, religion, and socioeconomic status [Greenwald, 1982]. The elevated prostatic cancer mortality was

restricted to men that started work in 1955–1964 at the age of 40 or older. A significantly reduced prostatic cancer mortality was found for men who started work in 1935–1944 at the age of 40 or older. Multiple comparisons always plague large studies, and it is very difficult to attach any significance to this observation.

Limited data suggest that exposure to phenoxy acid herbicides may be associated with soft tissue sarcoma [Hardell and Sandstrom, 1979] and non-Hodgkin's lymphoma (NHL) [Hardell et al., 1981; Hoar et al., 1986]. The earliest historical data on herbicide use, dating to 1952, indicate that 2,4-D and 2,4,5-T were used for control of weeds and brush along the highway right-of-way. The use of 2,4,5-T was discontinued in 1978. Anecdotal evidence suggests that many HMWs had substantial exposure to these and other herbicides. No deaths resulting from soft tissue sarcoma were observed in this cohort, whereas 1.4 were expected. Deaths caused by NHL were not precisely defined since the taxonomy for these malignancies has varied substantially over the last 40 years. The SMR for lymphomas not specified as Hodgkin's disease was elevated (SMR = 112) but not significant. Since these findings are based on limited numbers and no measure of individual exposure was available, their implication to the phenoxy acid herbicide question is unclear.

The natural history of melanoma represents a puzzling and inconsistent picture [Lee, 1982]. Although white populations with intense exposure to sunlight have increased risk of melanoma, outdoor workers do not appear to be at greater risk than comparable indoor workers. Highway maintenance work during the spring and summer is almost exclusively outdoors, with substantial exposure to the sun. Nearly three deaths due to melanoma were expected and none was observed. The typical HMW experience with steady exposure to the sun leads to a deep tan which may be protective.

In summary, this study has specifically evaluated the cancer mortality of a previously unstudied large group of workers. Although the overall mortality and all-cancer mortality were substantially reduced, plausible increases in leukemia and urologic cancer mortality were found. Since this was a cohort study of men who may have shared experiences other than just their work, the extent to which these findings are related to particular workplace exposures remains unknown. Case-control studies, environmental monitoring, and other studies of potential exposures are currently underway to assess the significance of the results reported here.

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REFERENCES

Aksoy M, Dincol K, Erdem S (1962): Acute leukemia due to chronic exposure to benzene. Am J Med 52:160–166.

Aksoy M, Erdem S, Dincol G (1976): Types of leukemia in chronic benzene poisoning. A study of thirty-four patients. Acta Haematol 55:65–72.

Armstrong BG, Kazantzis G (1985): Prostatic cancer and chronic respiratory and renal disease in British cadmium workers: A case control study. Br J Ind Med 42:540–545.

Bailar JC, Ederer F (1964): Significance factors for the ratio of a Poisson variable to its expectation. Biometrics 20:639–643.

Bender AP, Parker DL, Johnson RA, Anderson WA, Crozier MA, Williams AN, Marbury MC, Sigurdson E (1987): "The Minnesota Highway Maintenance Worker Study 1945–1984." Minneapolis, MN: Minnesota Department of Health.

Bender AP, Robison LL, Kashmiri SVS, McClain KL, Woods WG, Simthson WA, Heyn R, Finlay J, Schuman LM, Renier C, Gibson R (1988): No involvement of bovine leukemia virus in childhood acute lymphoblastic leukemia and non-Hodgkin's lymphoma. Cancer Res 48:2919–2922.

Bingham E, Falk HL (1969): Environmental carcinogens: The modifying effect of cocarcinogens on the threshold response. Arch Environ Health 19:779–783.

Bizzozero O, Johnson K, Ciocco A (1966): Radiation-related leukemia in Hiroshima and Nagasaki, 1946–1964. I. Distribution, incidence, and appearance-time. N Engl J Med 174:1095–1101.

Blair A, Fraumeni JF Jr, Mason TJ (1980): Geographic patterns of leukemia in the United States. J Chronic Dis 33:521–526.

Blair A, White DW (1985): Leukemia cell types and agricultural practices in Nebraska. Arch Environ Health 40:211–214.

Brandt HC, DeGroot PC, Molyneux MKB, Tindle PE (1985): Sampling and analysis of bitumen fumes. Ann Occup Hyg 29:27–80.

Caldwell GG, Heath CW (1976): Case clustering in cancer. South Med J 69:1598–1602.

Carpenter LM (1987): Some observations on the healthy worker effect. Br J Ind Med 44:289–291.

Checkoway H, Wilcosky T, Wolf P, Tyroler H (1984): An evaluation of the associations of leukemia and rubber industry solvent exposures. Am J Ind Med 5:239–249.

Cohen HJ, Huang ATF (1973): A marker chromosome abnormality. Occurrence in chloramphenicol-associated acute leukemia. Arch Intern Med 132:440–443.

Court-Brown W, Doll R (1965): Mortality from cancer and other causes after radiotherapy for ankylosing spondylitis. Br Med J 2:1327–1332.

Darby FW, Willis AF, Winchester RV (1986): Occupational health hazards from road construction and sealing work. Ann Occup Hyg 30:445–454.

Domiano SF, Vena JE, Swanson MK (1985): Gasoline exposure, smoking, and kidney cancer (letter). J Occup Med 27:398–399.

Flodin U, Fredriksson M, Persson B, Axelson O (1988): Chronic lymphatic leukaemia and engine exhausts, fresh wood, and DDT: A case-referent study. Br J Ind Med 45:33–38.

Fraumeni J (1969): Clinical epidemiology of leukemia. Semin Hematol 6:250–267.

Gallo RC (1985): The human T-cell leukemia/lymphotropic retroviruses (HTLV) family: Past, present, and future. Cancer Res 45:4524–4533.

Gardner MJ (1986): Considerations in the choice of expected numbers for appropriate comparisons in occupational studies. Med Lav 77:23–47.

Garshick E, Schenker MB, Munoz A, Segal M, Smith TJ, Woskie SR, Hammond SK, Speizer FE (1987): A case-control study of lung cancer and diesel exhaust exposure in railroad workers. Am Rev Respir Dis 135:1242–1248.

Goodman MT, Morganstein H, Wynder EL (1986): A case-control study of factors affecting the development of renal cell cancer. Am J Epidemiol 124:926–941.

Greenwald P (1982): Prostrate. In Schottenfeld D, Fraumeni JF Jr (eds): "Cancer Epidemiology and Prevention." Philadelphia: WB Saunders Company, pp 938–946.

Hammond EC (1966): Smoking in relation to death rates of one million men and women. Natl Cancer Inst Monogr 19:127–204.

Hammond EC, Selikoff IJ, Lawther PL, Seidman H (1976): Inhalation of benzypyrene and cancer in man. Ann NY Acad Sci 221:116–124.

Hardell L, Sandstrom A (1979): Case-control study: Soft-tissue sarcoma and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 711–717.

Hardell L, Eriksson M, Lenner P, Lundgren E (1981): Malignant lymphoma and exposure to chemicals especially organic solvents, chlorophenols and phenoxy acids: A case-control study. Br J Cancer 43:169–176.

Hart GD (1964): Leukaemia and phenylbutazone. Br Med J 2:569–571.

Hill ID (1972): Computing man years at risk. Br J Prev Soc Med 26:132–134.

Hoar S, Blair A, Holmes FF, Boysene D, Robel RJ, Hoover R, Fraumeni JF Jr (1986): Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. JAMA 256:1141–1147.

Horton AW, Christian GM (1974): Cocarcinogenic versus incomplete carcinogenic activity among aromatic hydrocarbons: Contrast between chrysene and benzo(b)triphenylene. JNCI 53:1017–1020.

Infante P, Wagoner J, Rinsky R, Young RJ (1977): Leukemia in benzene workers. Lancet 2:76–78.

Lee JAH (1982): Melanoma. In Schottenfeld D, Fraumeni JF Jr (eds): "Cancer Epidemiology and Prevention." Philadelphia: WB Saunders Company, pp 984–995.

Maizlish N, Beaumont J, Singleton J (1986): Mortality among transportation workers. Public Service Research and Dissemination Program. University of California, Davis. Final Report, September 30, 1986.

McLaughlin JK, Mandel JS, Blot WJ, Schuman LM, Mehl ES, Fraumeni JF Jr (1984): A population-based case-control study of renal cell carcinoma. JNCI 72:275–284.

McMichael AJ, Spirtas R, Kupper LL, Gamble JF (1975): Solvent exposure and leukemia among rubber workers. An epidemiologic study. J Occup Med 17:234–239.

McMichael AJ (1976): Standardized mortality ratios and the "healthy worker effect": Scratching beneath the surface. J Occup Med 18:165–168.

Monson RR (1974): Analysis of relative survival and proportional mortality. Comput Biomed Res 7:325–332.

Monson RR (1986): Observations on the healthy worker effect. J Occup Med 28:425–433.

Morrison AS, Cole P (1982): Urinary tract. In Schottenfeld D, Fraumeni JF Jr (eds): "Cancer Epidemiology and Prevention." Philadelphia: WB Saunders Company, pp 925–937.

Parker DL, Bender AP, Johnson RA, Scharber WK, Williams AN, Marbury MC, Mandel JS (1988): Minnesota highway maintenance worker cohort mortality study: Methods and noncancer mortality. Am J Ind Med 15:531–543.

Pike MC, Henderson BE (1980): Clustering of cancer cases. Natl Cancer Inst Monogr 53:47–50.

Rogot E (1974): Smoking and mortality among U.S. veterans. J Chronic Dis 27:189–203.

Ross RK, Shimizu H, Paganini-Hill A, Honda G, Henderson BE (1987): Case-control studies of prostatic cancer in blacks and whites in Southern California. JNCI 78:869–874.

Sandler DP, Collman GW (1987): Cytogenetic and environmental factors in the etiology of the acute leukemias in adults. Am J Epidemiol 126:1017–1032.

Severson RK (1987): Cigarette smoking and leukemia. Cancer 60:141–144.

Vena JE, Sultz HA, Carlo GL, Fiedler RC, Barnes RE (1987): Sources of bias in retrospective cohort mortality studies: A note on treatment of subjects lost to follow-up. J Occup Med 29:257–261.

Wallcave L, Garcia H, Feldman R, Lijinsky W, Shubik P (1971): Skin tumerigenesis in mice by petroleum asphalts and coal-tar pitches of known polynuclear aromatic hydrocarbon content. Toxicol Appl Pharmacol 18:41–52.

Waxweiler RJ, Beaumont JJ, Henry JA, Brown DP, Robinson CF, Ness GO, Wagoner JK, Lemen RA (1983): A modified life-table analysis system for cohort studies. J Occup Med 25:115–124.

Weed DL (1986): Historical roots of healthy worker effect. J Occup Med 28:343–347.

Wen CP, Tsai SP, Gibson RL (1983): Anatomy of the healthy worker effect: A critical review. J Occup Med 25:283–289.