The Mortality of Lead Smelter Workers: An Update

ABSTRACT

Objectives. Mortality studies of lead workers have shown excesses of nonmalignant renal disease and cerebrovascular disease. Animal studies and one human study have shown excess kidney cancer. We have updated a mortality study of male lead smelter workers (n = 1990).

Methods. An analysis was conducted using standard life table techniques. The updated analysis added 11 years of follow-up and 363 new deaths.

Results. The original study had found elevated but nonsignificant risks for kidney cancer, stroke, and nonmalignant renal disease, probably attributable to lead exposure. Deaths from accidents and nonmalignant respiratory disease were significantly elevated, but probably not as a result of lead exposure. In the updated study, no new deaths from nonmalignant renal disease occurred (9 observed, standardized mortality ratio = 1.21). Three more deaths from kidney cancer were observed, yielding a standardized mortality ratio of 1.93 (9 observed, 95% CI = 0.88, 3.67), which increased for those who had worked in areas with the highest lead exposure (8 observed, standardized mortality ratio = 2.39, 95% CI = 1.03, 4.71). Cerebrovascular disease remained elevated for those with more than 20 years of exposure (26 observed, standardized mortality ratio = 1.41, 95% CI = 0.92, 2.07).

Conclusions. This cohort with high lead exposure showed a diminishing excess of death from nonmalignant renal disease, a continued excess from kidney cancer, and an excess of cerebrovascular disease only in those with longest exposure to lead. (*Am J Public Health.* 1992;82:1641–1644)

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Introduction

Lead has long been recognized to induce nephropathy among heavily exposed workers.[1] Somewhat less certain are the relationships between lower level lead exposure and nephropathy and between lead exposure and hypertensive or cerebrovascular disease.[2] Soluble salts of lead (lead acetate, subacetate, and phosphate) have been shown to cause dose-related kidney cancer in animals when administered orally, subcutaneously, or intraperitoneally.[3] There have been two case reports of workers with lead poisoning who subsequently developed both nonmalignant and malignant renal disease.[4,5] The International Agency for Research on Cancer concluded that the evidence for the animal carcinogenicity of inorganic lead compounds is sufficient based on the observed kidney cancer, but it has labeled human evidence insufficient.[3]

The mortality of seven groups of lead-exposed workers has been studied (see Table 1).[6–12] The evidence to date supports an association between lead and chronic (nonmalignant) renal disease, with a number of studies also finding elevated cerebrovascular disease. For both outcomes, excesses appear confined to earlier calendar time periods, when exposures were presumably highest. Only one study has found an excess of kidney cancer,[8] but most other studies have had very limited power to detect an excess of this rare disease.

With this background, we extended the follow-up of the US lead smelter cohort previously studied by Selevan et al.[8] from 1977 through 1988. The a priori outcomes of principal interest were malignant and nonmalignant renal disease and cerebrovascular disease.

Materials and Methods

This cohort has been previously described.[8] Briefly, it consists of 1990 male hourly smelter workers who worked in a lead-exposed department for at least 1 year, with at least 1 day of employment at the smelter between 1940 and 1965 (the smelter operated in Idaho from 1917 to 1982). Race was not available from personnel records for most cohort members, who were assumed to be White. This assumption proved justified based on data from death certificates (982 of 985 decedents who had death certificates were White). No smoking data were available for the cohort.

This cohort was heavily exposed to lead. A 1975 National Institute for Occupational Safety and Health industrial hygiene survey showed average airborne lead concentrations of 3.1 mg/m^3, based on 203 personal 8-hour samples.[13] The Occupational Safety and Health Administration standard at the time was 0.20 mg/m^3, while the current standard is 0.05 mg/m^3.[14] Blood leads in 1976 averaged 56.3 μg/100 mL (n = 173, SD = 12.9) (National Institute for Occupational Safety and Health, unpublished data, 1976).

The cohort could have worked in any of 14 exposed departments or in nonex-

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TABLE 1—Prior Epidemiologic Studies of Lead Workers

Study/Year	Characteristics[a]	Results[b]
Malcolm and Barnett[6] (1982)	1898 battery workers, 1925–1976, cohort mortality, 50–60 μg/100 mL in 1965–1975 (n = 1391 in 1965, 1559 in 1975)	Renal (nonmalignant) SMR = 2.55* (11), cerebrovascular SMR = 1.28* (43) (for the high-exposure group only; the low-exposure group had no excess)
Cooper et al.[7] (1985)	4519 battery workers and 2300 production workers, 1947–1980, cohort mortality, 63 and 80 μg/100 mL over 1947–1972 (n = 1326 and n = 537, respectively)	Battery renal SMR = 2.22* (20), production renal SMR = 2.65* (8), battery lung cancer SMR = 1.09* (124), battery stomach cancer SMR = 1.68* (34)
Selevan et al.[8] (1985)	1987 smelter workers, 1940–1977, cohort mortality, 57 μg/100 mL in 1976 (n = 173)	Renal SMR = 192 (9), kidney cancer SMR = 204 (6), accidents SMR = 138* (56), nonmalignant respiratory disease SMR = 187* (32)
Gerhardsson et al.[9] (1986)	437 copper smelter workers, 1950–1981, cohort mortality, 58 and 34 μg/100 mL in 1950 and 1974 (n = 437)	Lung cancer SMR = 162 (8)
McMichael and Johnson[10] (1982)	241 lead poisoned workers, 1930–1977, proportionate mortality	Renal PMR = 3.06* (21), cerebrovascular PMR = 1.99* (16)
Davies[11] (1984)	57 lead poisoned workers, date of poisoning through 1981, cohort mortality	Renal SMR = 12.5* (3), cerebrovascular SMR = 4.09* (9)
Michaels et al.[12] (1991)	1261 typesetters, 1961–1984, cohort mortality, low levels, 10–20 μg/m^3 in air before 1970s, less thereafter	Cerebrovascular SMR = 1.35 (43) (increasing to 1.68* for those with more than 30 years of exposure)

[a]Population, follow-up period, design, and average blood lead level (number sampled) or air level if available.
[b]Cause and standardized mortality ratio (SMR) or proportionate mortality ratio (PMR) (number observed).
*P = .05.

TABLE 2—Description of Lead Cohort (n = 1990)

	No.	SD
Alive as of 1988 (%)	873 (43.9%)	...
Lost to follow-up (%)	89 (4.5%)	...
Dead (%)	1 028 (51.5%)	...
With certificate	990	...
Without certificate	38	...
Person-years at risk	57 615	...
Average length of employment, y	13.8	11.4
Average length of lead exposure, y	9.9	10.4
Average time of follow-up, y	32.2	12.5

Note. The average year of first exposure was 1946 (SD = 10.8); the average year of birth was 1916 (SD = 15.6). Three men were added to the earlier cohort[8] after correction of invalid dates of birth.

posed areas of the plant. High-lead departments were defined as those in which the average airborne lead concentrations during the 1975 survey exceeded 0.2 mg/m^3, or in which 50% or more of the jobs surveyed had average levels more than twice the existing standard. Men who had ever worked in high-lead jobs were analyzed as a subgroup.

Arsenic exposures in this cohort were relatively low, averaging 14 μg/m^3 in 1975 (n = 89).[13] The current Occupational Safety and Health Administration standard is 10 μg/m^3.[14] Cadmium exposures were also relatively low, averaging 113 μg/m^3 in 1975. The current standard is 200 μg/m^3.[14] Arsenic is associated with lung and skin cancers in humans, and cadmium is a suspected human lung carcinogen.[3] Chronic cadmium exposures may be associated with renal disease.[15] However, cadmium's role in causing clinical kidney damage is much less established than lead's, and exposures to lead were approximately 30 times higher at this plant than were exposures to cadmium.

Follow-up of the cohort was conducted via the Social Security Administration and the National Death Index. Any cohort members who were known to be alive after December 31, 1979 (when the National Death Index began), who had valid Social Security numbers, and who were not found to be dead via the National Death Index, were assumed to be alive through 1988.

Cohort analysis was conducted via traditional life table methods using the Life Table Analysis System of the National Institute for Occupational Safety and Health.[16] The US population was used a referent group. Significance testing and confidence intervals for standardized mortality ratios were calculated under the assumption that observed deaths were distributed as Poisson variables. A test for trend in standardized mortality ratios described by Breslow et al.[17] was used. Person-years at risk for cohort members began after they had completed 1 year of exposure but not earlier than 1940.

In addition to underlying cause of death analysis, multiple cause of death rates for the US population from 1960 onwards[16] were used for a comparison of the prevalence of nonmalignant renal disease on the death certificate in the cohort vs the referent population.

Results

A description of the cohort and the follow-up is presented in Table 2. Table 3 lists the mortality results for the whole cohort and for those who ever worked in a high-lead department. An excess of kidney cancer is apparent in Table 3 and is most strongly elevated in the high-lead group. A separate analysis of this high-lead group, excluding those who had ever worked in two departments with high cadmium exposure (n = 127), continued to show a kidney cancer excess (standardized mortality ratio = 2.62, 95% CI = 1.13, 5.16, eight observed). Local Idaho male rates for kidney

TABLE 3—Mortality Results for Entire Cohort and High Lead Exposure Subcohort

Cause (ICD-9 Code)	Entire Cohort (n = 1990) No. Observed	SMR	95% Confidence Interval	High Lead Exposure Subcohort (n = 1436) No. Observed	SMR	95% Confidence Interval
All cancers (140–208)	192	0.98	0.84, 1.12	137	0.98	0.81, 1.15
Stomach (151)	15	1.36	0.75, 2.24	10	1.28	0.61, 2.34
Colon (152–153)	9	0.48	0.22, 0.90	8	0.59	0.25, 1.16
Lung (162)	72	1.18	0.92, 1.48	49	1.11	0.82, 1.47
Prostate (185)	14	0.81	0.44, 1.36	10	0.84	0.40, 1.55
Kidney (189.0–189.2)	9	1.93	0.88, 3.67	8	2.39	1.03, 4.71
Bladder (188, 189.3–189.9)	9	1.93	0.88, 3.67	6	1.33	0.48, 2.90
Hematopoietic (200–208)	13	0.76	0.40, 1.30	9	0.73	0.33, 1.39
Ischemic heart disease (410–414)	320	0.94	0.84, 1.05	239	0.99	0.87, 1.12
Hypertension with heart disease (402, 404)	14	0.97	0.53, 1.63	12	1.18	0.60, 2.05
Hypertension with no heart disease (401, 403, 405)	6	1.73	0.63, 3.77	3	2.49	0.24, 3.52
Cerebrovascular disease (430–438)	74	1.05	0.82, 1.32	53	1.05	0.79, 1.37
Nonmalignant respiratory disease (460–519)	92	1.44	1.16, 1.77	67	1.46	1.13, 1.85
Emphysema (492)	27	2.20	1.45, 3.20	22	2.51	1.57, 3.80
Pneumoconioses and other respiratory (470–478, 494–519)	40	1.88	1.34, 2.56	28	1.81	1.20, 2.62
Acute kidney disease (580–581, 584)	1	0.91	0.02, 5.07	0	...	...
Chronic kidney disease (582–583, 585–587)	8	1.26	0.54, 2.49	7	1.55	0.62, 3.19
Accidents (E800–E949)	84	1.78	1.42, 2.21	61	1.81	1.39, 2.33
Transportation accidents (E800–E848, 929.0–929.1)	42	1.77	1.28, 2.40	31	1.84	1.25, 2.61
Falls (E880–E888, E929.3)	15	2.02	1.13, 3.34	9	1.70	0.77, 2.21
Other accidents (E890–E928, E929.4–E929.9)	25	1.88	1.22, 2.78	20	2.11	1.29, 3.27
All deaths	1028	1.07	1.00, 1.14	732	1.06	0.98, 1.14

Note. ICD-9 = *International Classification of Diseases, 9th version;* SMR = standardized mortality ratio.

cancer were approximately 14% less than US rates during the study period, so the use of Idaho rates would increase the kidney cancer standardized mortality ratios by about 14%.

The excess that had been previously observed for chronic renal disease was decreased in the updated data, as no new cases occurred during the extended follow-up period.

Deaths from accidents and nonmalignant respiratory disease (particularly the subcategory of emphysema and the subcategory including the pneumoconioses) were significantly elevated, reflecting previous findings for this cohort.

Table 4 provides the results by duration of exposure. Chronic renal disease was elevated among those with long exposure (standardized mortality ratio = 2.79, 95% CI = 0.75, 7.15). The kidney cancer excess did not show a consistent trend with either duration of exposure or time since first exposure (latter analysis not shown).

When we used US multiple cause of death rates after 1960 to analyze the prevalence of renal disease at death, the ratio of observed to expected occurrences on the death certificate for acute and chronic renal disease combined was unremarkable (standardized mortality ratio = 1.10, 24 observed).

Discussion

This study lack detailed data on lead exposures, detailed data on potential confounding exposures to cadmium and arsenic, and smoking data. However, we do have data indicating that this cohort was exposed to high levels of lead and that exposures to cadmium and arsenic were generally minor. Furthermore, many of the outcomes of a priori interest are not related to smoking.

The previously observed excess deaths due to accidents and nonmalignant respiratory disease continued to be significantly elevated in this cohort. However, a review of death certificates and employment applications indicated that these excesses were probably due to work in the mining industry rather than lead exposure.

Lung cancer and bladder cancer deaths showed nonsignificant elevations (standardized mortality ratios = 1.18 and 1.93, respectively). However, neither cancer was particularly elevated in the subcohort with high lead exposure. Neither cancer has been implicated in animal studies, and, with the exception of a single study with a lung cancer excess,[9] there is little epidemiologic evidence implicating these cancers. Both cancers are related to smoking, and excess smoking in the cohort may have contributed to their elevation.

Regarding a priori outcomes, the most important findings from this update are the persistence of the kidney cancer excess and the lowering of the nonmalignant renal disease excess. Cerebrovascular disease mortality was elevated only slightly overall. However, there was an increasing trend in standardized mortality ratios with increasing duration of exposure ($P = .07$).

The kidney cancer excess (standardized mortality ratio = 1.93), while based on small numbers (nine observed), is supported by the increase in the standardized mortality ratio in the subcohort with high lead exposure (standardized mortality ratio = 2.39). The kidney cancer excess was not clearly related to duration of exposure, but duration of exposure fails to account for intensity; thus, duration may not be a good indication of cumulative dose. The fact that animal studies show that lead

TABLE 4—Mortality Results for Selected Causes by Duration of Exposure, for the Entire Cohort

Cause (ICD-9 Code)	1–5 y SMR	1–5 y No. Observed	5–20 y SMR	5–20 y No. Observed	20+ y SMR	20+ y No. Observed
All cancers (140–208)	1.03	85	0.97	68	0.90	39
Stomach (151)	2.41*	10	0.73	3	0.72	2
Colon (152–153)	0.13	1	0.73	5	0.68	3
Lung (162)	1.25	34	1.17	25	1.02	13
Kidney (189.0–189.2)	1.97	4	1.82	3	2.05	2
Bladder (188, 189.3–189.9)	0.42	1	2.16	5	1.88	3
Ischemic heart disease (410–414)	1.02	137	0.92	115	0.86	68
Hypertension with heart disease (402, 404)	0.60	3	0.90	5	1.57	6
Hypertension with no heart disease (401, 403, 405)	1.54	2	1.51	2	2.38	2
Cerebrovascular disease (430–438)	0.83	21	1.01	27	1.41	26
Nonmalignant respiratory disease	1.43*	36	1.45*	34	1.44	22
Emphysema (492)	2.69*	13	1.81	8	1.99	6
Pneumoconioses and other respiratory (470–478, 494–519)	1.93*	17	2.38*	18	1.02	5
Chronic kidney disease (582–583, 585–587)	0.79	2	0.84	2	2.79	4
Transportation accidents (E800–E848, 929.0–929.1)	2.08*	27	1.39	11	1.43	4
Falls (E880–E888, E929.3)	2.37	7	1.42	4	2.45	4
Other accidents (E890–E928, E929.4–E929.9)	2.68*	18	1.49	7	0.00	0
All deaths	1.14*	450	1.00	350	1.06	228

Note. ICD-9 = *International Classification of Diseases, 9th version;* SMR = standardized mortality ratio.
*Significantly elevated at the .05 level (two-tailed).

causes kidney cancer lends strength to these findings. Kidney cancer is only weakly related to smoking, and excess smoking by this cohort would not be expected to lead to an appreciable excess.[18]

That a kidney cancer excess was not observed in other studies may be partly attributable to a lack of power in those studies due to small sample size. On the other hand, the study by Cooper et al.[7] did have high exposure and substantial sample size, yet the kidney cancer standardized mortality ratio was only 0.50 (10 observed). There is no obvious explanation for this discrepancy with our own findings.

The excess of nonmalignant renal disease observed in our data was concentrated in earlier calendar periods and among those with longest duration. Studies of other lead cohorts have also found that nonmalignant renal disease excesses were confined to earlier calendar periods, among those exposed to presumably high historical levels. □

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