on the Decline in Coronary
tality. Washington, DC: Na-
Health, 1979:116–23.
ne in hospitalizations for cor-
and stroke: the Kaiser-Per-
e in north California, 1971–
, Feinleib M, eds. Proceedings
on the Decline in Coronary
tality. Washington, DC: Na-
Health, 1979:109–15.
mortality in coronary heart
rosis 1981;1:312–25.
nt decline in ischemic heart
Ann Intern Med 1979;91:630–

Council B, et al. Cardiovascular
atterns in Georgia and North
alth Rep 1966;75:841–51.
ic patterns in the risk of dying
ors, ages 35–74 years, United
Rockville, MD: National Cen-
istics, 1980. (Vital and health
no. 18).
ic areas of the United States.
ess of Glencoe, 1961.
A, Sauer H, et al. Death rates
olitan and other areas. Public
:759–66.
ns in heart disease mortality
New York State. Public Health
l.
l J. Health consequences of
The effect of urbanization on
ease mortality in rural resi-
is 1964;17:167–77.
edical care, better health?
rban Institute, 1982.
SAS user's guide. Cary, NC:
1979.
ry mortality: what is going on?
45–6.
rise and fall of ischemic heart
80;243:53–9.
RJ, Thom T. The changing
ic heart disease. J Cardiovasc
.
l. Cardiovascular disease death
in Georgia. J Med Assoc Ga

W. The downward trend in
ease mortality. Ann Rev Med

AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 122, No. 4
Printed in U.S.A.

MORTALITY OF LEAD SMELTER WORKERS

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To examine patterns of death in lead smelter workers, a retrospective analysis of mortality was conducted in a cohort of 1,987 males employed between 1940 and 1965 at a primary lead smelter in Idaho. Overall mortality was similar to that of the United States white male population (standardized mortality ratio (SMR) = 98). Excess mortality, however, was found from chronic renal disease (SMR = 192; confidence interval (CI) = 88–364), and the risk of death from renal disease increased with increasing duration of employment, such that after 20 years employment, the standardized mortality ratio reached 392 (CI = 107–1,004). Excess mortality was also noted for nonmalignant respiratory disease (SMR = 187, CI = 128–264). Eight of 32 deaths in this category were caused by silicosis; at least five workers who died of silicosis had been miners for a part of their lives. An additional 11 deaths resulted from tuberculosis (SMR = 139; CI = 69–249); in six of these cases, silicosis was a contributory cause of death. Cancer mortality was not increased overall (SMR = 95; CI = 78–114). An increase, however, was noted for deaths from kidney cancer (six cases; SMR = 204; CI = 75–444). Finally, excess mortality was noted for injuries (SMR = 138; CI = 104–179); 13 (23%) of the 56 deaths in this category were caused by mining injuries. The data from this study are consistent with previous reports of increased mortality from chronic renal disease in persons exposed occupationally to lead.

kidney neoplasms; lead; nephritis; nephrosis; silicosis

Primary lead smelters are large industrial complexes, whose function is to extract lead from ore. In the traditional smelting process, lead sulfide ore (galena) is first separated from nonmetallic rock by differential flotation in an ore concentrator (1). The ore is then roasted in an oxidizing (sintering) furnace, where sulfur is driven off principally as sulfur dioxide (SO_2). The roasted ore is charged with coke into a blast furnace, where lead is separated from silica, iron, calcium, copper, and other impurities through regulation of temperatures around the melting point of lead. The resulting lead bullion is further refined to remove trace metals. Lead ingots of greater than 99.9 per cent purity constitute the major final product, but modern smelters may also produce commercial quantities of cadmium, zinc, copper, sulfuric acid, gold, and silver.

Occupational exposures to lead in pri-

Received for publication June 4, 1984, and in final form January 28, 1985.

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The authors acknowledge the generous assistance provided in this investigation by the following persons: Clorinda Battaglia, Edith Dodd, Judy Edelbrock, and their colleagues at NIOSH; Cynthia Forbes, Kay Woods, Pat Cruz, Don Vickars, and Tom McKenna of Westat, Inc.; and Janet M. Wick, Chief, Bureau of Vital Statistics, Idaho Department of Health and Welfare.

mary smelting are typically heavy. Workers are also exposed to zinc, cadmium, and arsenic as well as to SO_2, and in some departments to airborne free silica. Although lead intoxication occurs with considerably lower frequency than in the past (2), cases of lead poisoning continue to be reported in smelter workers (3). The tissues principally affected are those of the hematopoietic system, the brain and peripheral nerves, the kidneys, the gastrointestinal tract, and the testes. The corresponding manifestations of toxicity include anemia (3), peripheral neuropathy (4, 5), chronic nephropathy which may result in renal failure (3, 6–9), abdominal colic (3, 10), and possibly decreased male fertility (11). Hypertension, although not a constant finding in previous studies, has been reported in association with occupational lead exposure (12–14); it is hypothesized to be a consequence of renal injury.

Mortality studies of lead smelter and battery workers have consistently found excess deaths from chronic renal disease, particularly in heavily exposed long-term workers (15–18). Excess deaths from cerebrovascular disease (12, 16, 18) and from other forms of hypertensive vasculopathy (15) have also been noted. Excess mortality from cancer has not been a constant finding (12, 15–17), although lead is a mutagen (19), an animal carcinogen (20–25), and has been associated in two case reports of lead workers with primary renal carcinoma (26, 27).

In this report, we present the results of a retrospective analysis of mortality in a cohort of workers employed at a large lead concentrator and smelter in Idaho. Exposures to lead at this plant had frequently been above established standards (28, 29), and a previous medical survey had found evidence of lead toxicity (30). We were particularly interested in examining mortality due to nephritis, hypertensive vascular disease, renal cancer, and lung cancer.

Methods

The study population consisted of all white male hourly workers who were employed between January 1, 1940 and December 31, 1965 at the Bunker Hill ore concentrator and primary lead smelter in Kellogg, Idaho, and who worked there for at least one year. Also included were all male hourly workers employed in the same time period for whom data on race were not available (77.5 per cent of the work force); these workers were considered white for the purposes of this analysis, since it was known that in 1975 at least 96 per cent of the work force had been white. Data on the study population were derived from personnel records on 34,124 employees which were provided to us by smelter management. This record set included data on concentrator and smelter workers as well as on workers in other facilities operated by the company; it also included information on a number of short-term workers who were employed for less than one year.

Many of the study population lived in towns located within a few miles of the smelter. Those towns were heavily contaminated by airborne heavy metal emissions from the plant, and those workers were therefore at risk of both extraoccupational as well as occupational exposure to lead. Also, a large, although not precisely defined, number of cohort members had worked for a part of their lives as underground, hard-rock miners, principally in the lead-zinc-silver mines of the Coeur d'Alene district of northern Idaho. These workers were potentially exposed to the hazards of both mining and smelting.

Vital status of each cohort member was ascertained through December 31, 1977 by examination of records maintained by the Social Security Administration, the Veterans Administration, the Post Office address correction service, state vital statistics offices, the Internal Revenue Service, and state motor vehicle bureaus. For individuals not located through these sources, other means of ascertainment were employed, such as review of city directories. Workers with unknown vital status were considered alive at the end of the study;

this conservative procedure tends to produce a slight underestimation of observed mortality.

Death certificates were obtained from state vital records offices. Underlying causes of death were coded by a qualified nosologist, according to the revision of the *International Classification of Diseases* (ICD) in effect at the time of death; all codes subsequently were converted to the Seventh Revision.

To evaluate in further detail the effects on mortality of occupational exposures to lead and to other metals, we developed a series of exposure definitions from data obtained in an industrial hygiene survey conducted at the smelter in 1975 (28) (table 1). We defined high-lead departments as follows: those in which the mean level of airborne lead exposure for all jobs examined was above the then current standard of the Occupational Safety and Health Administration of 200 $\mu g/m^3$; or those in which 50 per cent or more of the jobs examined had mean airborne lead exposures greater than twice that standard.

Because workers in some high-lead departments were also potentially exposed to cadmium, zinc, or arsenic, we divided the high-lead departments into those with and without high potential for exposure to other metals. Departments with relatively high exposure to lead and relatively low exposure to other metals were termed "high-lead/low-other" departments and were distinguished from departments with mixed exposures, which were defined as follows: those in which workers in 50 per cent or more of the jobs examined were exposed to airborne cadmium, zinc, or arsenic in concentrations above any of the then current standards (table 1); or those in which workers in 25 per cent or more of the jobs examined were exposed to airborne cadmium, zinc, or arsenic in concentrations more than twice those standards.

To analyze the mortality of the study population, we employed a modified life table program developed by the National Institute for Occupational Safety and Health (31). Person-years of observation were tabulated by five-year calendar time periods and age groups, as well as by exposure and latency intervals. We examined separately the effect of employment in high-lead and high-lead/low-other departments. Tabulation of person-years for these two subgroups began with the worker's first employment in qualifying departments. In the high-lead/low-other group, to eliminate from the analysis the possible effects of exposures to metals other than lead, we "censored" from the life table those workers who had moved from high-lead/low-other departments to other high-lead departments; that is, person-years for such workers were counted for the high-lead/low-other departments only until their first potential exposure to other agents. After that time, neither their person-years nor their deaths contributed to the high-lead/low-other analysis. For each cause of death, comparison was made between the number of deaths observed in the cohort and the number expected on the basis of sex, age, race, and calendar time period for the United States white male population, according to data published annually by the National Center for Health Statistics and the US Census Bureau. Standardized mortality ratios (SMRs) were computed for each cause of death.

Confidence limits for standardized mortality ratios were determined using exact methods based on a Poisson distribution (32). Examination of trends in standardized mortality ratios was performed using a χ^2 trend test with 1 df, as developed by Breslow et al. (33). Because standardized mortality ratios, calculated by indirect standardization, have different underlying age distributions and because increasing age is correlated in most instances with increases in latency and exposure, these trend analyses may conceivably be measuring effects due to interactions of occupational factors with age as well as effects due solely to increases in latency or in

TABLE 1

Airborne exposures to heavy metals, by department and job title, Bunker Hill smelter, Kellogg, Idaho, 1975*

Department	Lead			Cadmium			Zinc			Arsenic		
	Range (μg/m)	No. of job titles examined	% over standard (% 2 × standard)	Range (μg/m)	No. of job titles examined	% over standard (% 2 × standard)	Range (μg/m)	No. of job titles examined	% over standard (% 2 × standard)	Range (μg/m)	No. of job titles examined	% over standard (% 2 × standard)
Concentrator	23–200	6	0 (0)	<1–2 Dust	6	0 (0)	17–70	6	0 (0)	<1–4	10	0 (0)
Charge preparation	1,200–15,000	9	100 (100)	18–970 Dust	9	56 (33)	54–210,000	8	38 (25)	1–12	4	0 (0)
Sinter plant	7,900–17,000	5	100 (100)	47–360 Dust	5	40 (0)	1,100–2,900	5	0 (0)	23–51	3	0 (0)
Blast furnace	800–22,000	5	100 (100)	11–225 Fume	5	40 (20)	180–2,900	5	0 (0)	7–32	4	0 (0)
Slag fuming furnace	79–2,100	9	89 (44)	<1–9 Fume	9	0 (0)	75–19,000	9	22 (11)	<1–5	7	0 (0)
Lead refinery	170–550	3	66 (66)	<1–2 Fume	3	0 (0)	55–470	3	0 (0)	18–200	3	0 (0)
Casting and loading	144–409	6	75 (25)	<1–8 Fume	6	0 (0)	NA†			<1–3	6	0 (0)
Cadmium refinery	1,200–4,900	2	100 (100)	660–2,600 Dust	2	100 (100)	110–290	2	0 (0)	NA		
Silver refinery	260–690	3	100 (66)	1–3 Dust	3	0 (0)	620–810	2	0 (0)	8–8	2	0 (0)
Materials recovery	960–56,000	4	100 (100)	<2–3,200 Dust	5	40 (20)	22–8,400	5	20 (0)	10–55	2	0 (0)
Maintenance	36–9,000	15	80 (73)	2–170 Dust	17	0 (0)	<2–1,800	14	0 (0)	<1–52	7	0 (0)
OSHA standard at time of survey	200			Dust 200 Fume 100			5,000			500		
Current OSHA standard	50			Dust 200			5,000			10		

* All data on airborne exposures are based on results of eight-hour time-weighted average (TWA_8) samples. Several such samples were collected for each job title (28).
† NA, not available.

duration of exposure. The magnitude of such potential confounding depends on the age distributions in the strata under examination.

RESULTS

The study population consisted of 1,987 white male hourly workers (table 2). At the end of the study period (December 31, 1977), 1,281 (64.5 per cent) of this cohort were alive, 665 (33.4 per cent) were deceased, and 41 (2.1 per cent) were lost to follow-up. Unfortunately, 64 (9.6 per cent) of the 665 death certificates could not be located at state vital records offices, even after provision of supplementary information by the Social Security Administration as to place of death. These deaths were considered to be of unknown cause, a conservative procedure which produces some underestimation of observed case-specific mortality.

The age-adjusted overall mortality of the cohort was approximately equal to that of the United States white male population ("all causes" SMR = 98) (table 3). Despite this absence of overall excess, a positive trend was evident between the all causes standardized mortality ratio and the length of the interval (latency) since first occupational exposure to lead (for the total population, $p = 0.05$; for the high-lead/low-other group, $p = 0.007$) (table 4). This positive trend appears to reflect an upward trend over time in mortality from cardiovascular disease (table 4), a tendency which may reflect a decrease in the strength of the "healthy worker effect" with aging of the population.

TABLE 2

Cohort vital status, Bunker Hill smelter, Kellogg, Idaho, December 31, 1977

	Study cohort members	
	n	%
Known to be alive	1,281	64.5
Known to be deceased	665	33.4
Death certificate obtained	601	30.2
Death certificate outstanding	64	3.2
Not known to be alive or deceased	41	2.1
Total	1,987	100.0

Renal disease

Excess mortality was observed for chronic, unspecified nephritis and nephrosis (nine cases; SMR = 192; confidence interval (CI) = 88–364) (table 3). When mortality from this cause was examined by duration of occupational exposure to lead and by latency interval since first exposure, positive dose-response relationships were evident (table 4). For those workers with more than 20 years exposure, the standardized mortality ratio for chronic renal disease was 392 (CI = 107–1,004), and for those with more than 20 years latency, the standardized mortality ratio was 315 (CI = 127–649).

Respiratory disease

Elevated mortality was observed for "other nonmalignant respiratory diseases" (32 cases; SMR = 187; CI = 128–264), a category which includes emphysema and the occupational respiratory diseases (table 3). Eight of the 32 deaths were due to silicosis; in five of these eight cases, mining was listed on the death certificate as the "usual" occupation of the deceased worker.

In addition, we found that 11 deaths in this population were caused by tuberculosis (SMR = 139; CI = 69–249) (table 3). Further examination of these death certificates indicated that silicosis was listed as a contributory cause of death in six workers; four of these workers had died of silicotuberculosis.

Vascular disease

Cerebrovascular disease mortality was not elevated (SMR = 84) (table 3). Standardized mortality ratios for cerebrovascular disease, however, tended to increase with increasing duration of employment ($p = 0.002$; high-lead/low-other group, $p = 0.07$), and to a lesser extent with increasing

		(100)	Dust		(20)			(0)			(0)		
Maintenance	36–9,000	15	80 (73)	2–170 Dust	17	0 (0)	<2–1,800	14	0 (0)	<1–52	7	0 (0)
OSHA standard at time of survey	200			Dust 200 Fume 100			5,000			500		
Current OSHA standard	50			Dust 200			5,000			10		

* All data on airborne exposures are based on results of eight-hour time-weighted average (TWA_8) samples. Several such samples were collected for each job title (28).
† NA, not available.

TABLE 3

Age-adjusted mortality experience of workers with at least one year of occupational exposure to lead, Bunker Hill smelter, Kellogg, Idaho, 1977

Cause of death (ICD* code)	Entire cohort			High-lead exposure areas			High-lead/low-other exposure areas§		
	Deaths observed	SMR†	(CI)‡	Deaths observed	SMR	(CI)	Deaths observed	SMR	(CI)
All tuberculosis (001–019)	11	139	(69–249)	1			1		
All cancers	116	95	(78–114)	81	96	(76–119)	72	104	(81–131)
Digestive organs and peritoneum (150–159)	30	77	(52–110)	19	71	(43–111)	17	77	(45–123)
Respiratory system (160–164)	41	111	(80–151)	28	109	(72–157)	25	120	(78–177)
Male genital organs (177–179)	7	69	(28–143)	6	86	(31–187)	5	88	(28–205)
Urinary organs (180–181)	12	169	(87–295)	9	183	(84–349)	8	199	(86–394)
Kidney (180)	6	204	(75–444)	5	245	(81–583)	5	301	(98–703)
Bladder and other urinary organs (181)	6	144	(53–314)	4	139	(38–353)	3	127	(26–371)
Diseases of the central nervous system (330–334)	46	84	(61–112)	32	84	(57–119)	29	94	(63–135)
Diseases of the circulatory system (400–468)	246	78	(69–88)	166	76	(65–88)	148	83	(70–98)
Diseases of the respiratory system (470–527)	47	125	(92–166)	30	115	(78–164)	27	127	(84–184)
Other respiratory diseases (510–527)	32	187	(128–264)	23	194	(122–290)	21	217	(134–331)
Diseases of the digestive system (540–581)	12	51	(26–89)	9	55	(25–104)	9	68	(31–129)
Diseases of the genitourinary system (590–652)	9	93	(42–177)	7	104	(42–214)	4	73	(20–186)
Chronic and unspecified nephritis and other renal sclerosis (591–594)	9	192	(88–364)	7	217	(88–451)	4	159	(44–410)
Accidents (800–962)	56	138	(104–179)	41	146	(105–198)	34	151	(105–211)
All other	57	88	(67–114)	42	93	(67–126)	36	98	(69–136)
Death certificates not received	65			44			41		
Total	665	98	(91–106)	453	97	(88–106)	401	105	(95–116)
Person-years	47,916.8			33,037.5			26,382.6		

* ICD, *International Classification of Diseases*, Seventh Revision.

† SMR, standardized mortality ratio (observed/expected) × 100; not calculated for observed number of deaths less than two.

‡ CI, 95% confidence interval.

§ Workers in lead exposure areas with relatively low exposure to other agents.

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* ICD, *International Classification of Diseases*, Seventh Revision.
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‡ CI, 95% confidence interval.
§ Workers in lead exposure areas with relatively low exposure to other agents.

TABLE 4

Age-adjusted mortality experience for selected causes of death, by duration of occupational exposure to lead and latency interval since first exposure, Bunker Hill smelter, Kellogg, Idaho, 1977

Cause of death (ICD* code)	Duration of exposure (years)									Latency interval (years)								
	<5			5-19			≥20			<5			5-19			≥20		
	Observed	SMR†	(CI)‡	Observed	SMR	(CI)	Observed	SMR	(CI)	Observed	SMR	(CI)	Observed	SMR	(CI)	Observed	SMR	(CI)
All cancers	44	90	(66-121)	43	96	(69-129)	29	102	(69-147)	3	76	(16-221)	28	73	(49-106)	85	106	(85-131)
Trachea, bronchus, and lung (162-163)	16	111	(64-181)	15	120	(67-198)	10	131	(63-241)	0			9	90	(41-170)	32	135	(93-191)
Kidney (180)	2	165	(20-597)	3	278	(57-812)	1			1			1			4	214	(58-548)
Diseases of the central nervous system: stroke (330-334)	9	47	(21-88)	16	75	(43-122)	21	146	(90-223)	0			8	53	(23-105)	38	99	(70-135)
Diseases of the circulatory system (400-468)	91	76	(61-93)	89	75	(60-92)	66	87	(67-111)	2	20	(2-71)	64	66	(51-84)	160	87	(74-100)
Arteriosclerotic heart disease (420)§	72	79	(62-99)	72	84	(66-106)	44	82	(60-111)	1			49	74	(55-98)	138	86	(72-101)
Hypertension with heart disease (440-443)§	1			2	52	(6-188)	3	116	(24-340)	0			0			6	105	(38-228)
Hypertension without heart disease (444-447)§	1			1			1			0			1			2	120	(15-433)
Other respiratory diseases (510-527)	12	179	(93-313)	13	208	(110-355)	7	168	(69-355)	0			12	300	(155-524)	20	164	(100-254)
Nephritis and nephrosis (591-594)	3	160	(33-469)	2	112	(14-404)	4	392	(107-1,004)	0			2	98	(12-352)	7	315	(127-649)
Accidents (800-962)	34	161	(111-225)	17	121	(71-194)	5	91	(30-213)	6	117	(43-254)	34	175	(121-244)	16	99	(57-161)
Transportation (800-866)	19	162	(97-253)	9	130	(59-246)	4	170	(46-436)	4	125	(34-319)	18	167	(99-264)	10	142	(68-261)
Other (870-962)	15	160	(89-264)	8	112	(48-221)	1			2	64	(12-372)	16	185	(105-300)	6	66	(24-145)
Total for all causes	265	98	(87-111)	232	92	(80-104)	168	109	(93-127)	19	65	(39-101)	208	94	(82-108)	438	103	(93-113)

* ICD, *International Classification of Diseases*, Seventh Revision.
† SMR, standardized mortality ratio (observed/expected) × 100; not calculated for observed number of deaths less than two.
‡ CI, 95% confidence interval.
§ Because of changes in ICD coding, these data refer only to deaths occurring after 1950.

latency (p = 0.07; high-lead/low-other group, p = 0.07) (table 4).

Mortality from diseases of the circulatory system occurred at a lower frequency than expected (SMR = 78; CI = 69–88) (table 3). Mortality from circulatory disease, however, tended to increase with increasing latency (p = 0.006) (table 4).

Cancer

Overall mortality from cancer (all anatomic sites) was not elevated (SMR = 95). Elevated standardized mortality ratios, however, were noted for kidney cancer (SMR = 204) (table 3). No substantial excess was observed in mortality from respiratory cancer (SMR = 111) (table 3).

Injuries

An excess of deaths due to injuries was observed in this cohort (SMR = 138; CI = 104–179) (table 3). Twenty-two (39.2 per cent) of the 56 deaths in this category were due to occupational injuries. The majority of these deaths, however, were associated with underground mining and not with employment at the smelter. Six were caused by suffocation and smoke inhalation in the Sunshine Mine disaster at Kellogg, Idaho, May 2, 1972. Another seven of these deaths were caused by various other mining episodes.

Discussion

This analysis of mortality in workers exposed to lead at the Bunker Hill smelter was prompted by investigations which had found lead contamination in the environment surrounding the smelter (34) and increased lead absorption, anemia, and neurologic impairment among children in adjacent communities (35). The present study was undertaken in conjunction with an industrial hygiene evaluation (28) and a cross-sectional medical survey (30).

The major finding was the observation of excess mortality from chronic renal disease. This effect was most strongly evident in long-term lead workers (table 4). Nephritis has been recognized as a component of occupational lead intoxication since the late nineteenth century (36, 37). Although the natural history and dose-response relationships for lead nephropathy are less well understood than those for other aspects of chronic lead poisoning, it appears that nephropathy is a consequence of prolonged, relatively high-dose exposure to lead (3, 6–9, 37). In previous mortality studies, deaths from lead nephropathy have tended to occur in workers with longest duration of exposure to lead (12, 16, 18) and in those who had suffered clinical lead poisioning (17).

The epithelial lining cells of the proximal tubules appear to be the tissue in the kidneys most highly sensitive to lead. The first histologically demonstrable effect of lead in the kidneys is the formation in these cells of densely staining intranuclear inclusion bodies (9), which have been shown to be comprised of a lead-protein complex (37). With continuing exposure, irreversible interstitial renal fibrosis develops (9). The end stage of lead nephropathy is chronic renal failure, characterized pathologically by interstitial fibrosis (38) and by atrophy and cystic dilatation of the tubules with relative sparing of the glomeruli (37). In some instances, lead nephropathy has been reported to be associated with hyperuricemic gout (8), possibly the result of a lead-induced defect in the tubular secretion of uric acid. Lead workers with nephropathy have been shown to have increased quantities of lead in bone and to excrete increased amounts of lead in urine following chelation challenge (38, 39), compared with lead workers without nephropathy or with unexposed comparison subjects. The finding in the present study of increased mortality from chronic nephritis corroborates the results of four previous epidemiologic analyses of lead workers (15–18).

The present study also found increased mortality from renal cancer (six cases; SMR = 204; CI = 75–444). Lead has been found in experimental studies in rats, mice,

and hamsters to produce both chronic renal disease and renal tumors (20–24, 40, 41). Although levels of lead exposure in those studies far exceeded the maximum doses tolerated by man and caused gross morphologic damage to the kidneys, positive dose-response relationships were observed between lead dose and tumor incidence; also, the interval from onset of exposure to tumor formation was reduced in the more heavily exposed animals (23). Two recent case reports have noted primary renal tumors in association with chronic nephritis in long-term lead workers (26, 27). Excess mortality from renal cancer has not been observed in previous epidemiologic studies of lead workers. Pending epidemiologic corroboration, the present finding must be interpreted with caution.

Death rates from both silicosis and tuberculosis were found to be elevated in this study; in six (55 per cent) of 11 workers who died of tuberculosis, silicosis was also noted to be present, and four of these death certificates recorded a diagnosis of silicotuberculosis. Similar findings have not been reported in previous mortality studies of smelter workers (12, 15–18), and the report by Cooper (15) noted a standardized mortality ratio for tuberculosis (all sites) in smelter workers of only 23. The present findings may reflect occupational exposure to silica in the concentrator and charge preparation departments of the smelter, where limited air sampling detected several exposures to silica dust in concentrations above the Occupational Safety and Health Administration standard (28). A more likely explanation, however, is that many workers in this cohort appear to have had occupational exposure to silica in underground, hard-rock mining, a common form of employment in northern Idaho. Mining was recorded on death certificates as usual occupation for five of the eight deaths due to silicosis encountered in this study. Underground miners have long been known to be at increased risk of death from silicosis and tuberculosis (42).

In contradistinction to several previous studies of lead workers (12, 16, 17), this analysis did not find increased mortality from cerebrovascular or hypertensive vascular disease. Only slight upward trends in standardized mortality ratios for cerebrovascular accidents were noted with increasing duration of employment and with increasing latency. There is no obvious explanation for the differences between these results and those of previous studies.

A limitation in the present study lies in the definition of exposure. Although we attempted to define exposure by classifying workers according to 1) the duration of their employment, 2) the length of the latency interval since their first employment, and 3) their assignment to high-exposure departments (28), each of those categorizations is at best a relatively crude surrogate measure of actual exposure. In no way do these measures take cognizance of individual differenes in work practices, in respirator use, or in extraoccupational exposures to heavy metals, a form of exposure which could have been quite substantial for workers living in some neighborhoods near this smelter (34, 35). A likely consequence of the insensitivity of our measures of exposure is that we have underestimated the full range of exposures to lead and to other heavy metals which existed within this cohort. Had we been able to identify more precisely those members of the cohort who had heaviest cumulative exposures, we might have been able to define more precisely the effects of such exposures on mortality.

Two further limitations derive from our use of the entire United States white male population as a basis for calculating expected mortality. In the first instance, most populations of workers are healthier than the general population, because the latter includes numbers of chronically ill or otherwise unemployable persons. Consequently, comparison of the mortality experience of a working population with that of a general population produces an apparent deficit in

mortality, the so-called healthy worker effect (43). This effect tends to be strongest in the younger age groups and to diminish with increasing age (43). This diminution may reflect erosion in health as a consequence of hazardous work. Arguably, such erosion may account for the apparent upward trend for mortality from cardiovascular disease as well as for overall mortality which was observed in the present cohort with increasing latency since first employment. Resolution of the issues surrounding the healthy worker effect will require the development of life table programs which use the mortality experience of blue-collar-employed populations as a basis for computing expected mortality; such programs are currently under development in a joint effort between the National Cancer Institute and the National Institute for Occupational Safety and Health.

The second potential limitation stemming from our use of the entire US population and a basis of comparison is that this approach may obscure regional differences in mortality and thus distort calculated standardized mortality ratios. To examine this issue, we obtained data on cause-specific deaths for the state of Idaho for cancer for the years 1950–1977 and for other causes of deaths for the years 1962–1977. We found that age-adjusted Idaho rates for those years were 27.7 per cent higher than US rates for deaths due to injury and 54.2 per cent lower for deaths due to tuberculosis. However, for deaths due to chronic and unspecified nephritis and for deaths due to kidney cancer, the Idaho and US rates were, respectively, within 5 per cent and 10 per cent of each other. Thus, the US rates provide an acceptable basis for calculating expected mortality due to renal disease in the population of Idaho.

The statistical power of this study to detect increases in mortality depended upon the outcome under study and varied widely according to the background frequency of each condition. Based on the equations of Beaumont and Breslow (44), the power of this study to have detected a doubling in expected mortality for lung cancer was 98; for stroke 99.8; and for nonmalignant respiratory diseases 99.8. The power to detect doubling in mortality, however, was much lower for other causes of death: for cancer of the urinary organs 51; for cancer of the bladder 36; for kidney cancer 28; and for nephritis and nephrosis 44.

In summary, the major finding of this study was the observation of excess mortality due to chronic renal disease in long-term lead workers. This finding corroborates the results of previous mortality studies of lead workers (12, 15–18). The study also found an increase in mortality for renal cancer. This finding is consistent with the results of experimental studies in animals, but has not previously been encountered in an epidemiologic analysis.

References

1. Howe HE. Lead. In: Kirk-Othmer encyclopedia of chemical technology. 3rd ed. Vol 14. New York: John Wiley & Sons, 1978:98–139.
2. Hunter D. The diseases of occupations. 4th ed. Boston: Little, Brown & Co, 1969.
3. Baker EL Jr, Landrigan PJ, Barbour AG, et al. Occupational lead poisoning in the United States: clinical and biochemical findings related to blood lead levels. Br J Ind Med 1979;36:314–22.
4. Araki S, Honma T. Relationships between lead absorption and peripheral nerve conduction velocities in lead workers. Scand J Work Environ Health 1976;4:225–31.
5. Seppalainen AM, Tola S, Hernberg S, et al. Subclinical neuropathy at "safe" levels of lead exposure. Arch Environ Health 1975;30:180–3.
6. Wedeen RP, Maesaka JK, Weiner B, et al. Occupational lead nephropathy. Am J Med 1975; 59:630–41.
7. Lilis R, Gavrilescu N, Nestorescu B, et al. Nephropathy in chronic lead poisoning. Br J Ind Med 1968;25:196–202.
8. Ball GV, Sorensen LB. Pathogenesis of hyperuricemia in saturnine gout. N Engl J Med 1969; 280:1199–1202.
9. Goyer RA, Rhyne BC. Pathological effects of lead. Int Rev Exp Pathol 1973;12:1–77.
10. Dahlgren J. Abdominal pain in lead workers. Arch Environ Health 1978;21:156–9.
11. Lancranjan I, Popescu HI, Gavanescu O, et al. Reproductive ability of workmen occupationally exposed to lead. Arch Environ Health 1975; 30:396–401.
12. Dingwall-Fordyce I, Lane RE. A follow-up study of lead workers. Br J Ind Med 1963;20:313–15.
13. Emmerson BT. Chronic lead nephropathy: the

dy to have detected a
d mortality for lung
oke 99.8; and for non-
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ing in mortality, how-
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RENCES

Kirk-Othmer encyclopedia of
3rd ed. Vol 14. New York:
978:98–139.
es of occupations. 4th ed.
n & Co, 1969.
gan PJ, Barbour AG, et al.
isoning in the United States:
ical findings related to blood
Med 1979;36:314–22.
Relationships between lead
neral nerve conduction veloc-
s. Scand J Work Environ
l.
la S, Hernberg S, et al. Sub-
t "safe" levels of lead expo-
lealth 1975;30:180–3.
a JK, Weiner B, et al. Occu-
ropathy. Am J Med 1975;

N, Nestorescu B, et al. Ne-
ic lead poisoning. Br J Ind
2.
B. Pathogenesis of hyperuri-
gout. N Engl J Med 1969;

. Pathological effects of lead.
1973;12:1–77.
nal pain in lead workers. Arch
8;21:156–9.
scu HI, Gavanescu O, et al.
of workmen occupationally
Arch Environ Health 1975;

Lane RE. A follow-up study
J Ind Med 1963;20:313–15.
ronic lead nephropathy: the

diagnostic use of calcium EDTA and the association with gout. Australas Ann Med 1963;12:310–24.
14. Cramer K, Dahlberg L. Incidence of hypertension among lead workers: a follow-up study based on regular control over 20 years. Br J Ind Med 1966;23:101–4.
15. Cooper WC. Mortality in employees of lead battery plants and lead-producing plants. Presented at the XXI International Congress on Occupational Health, Dublin, Republic of Ireland, September 1984.
16. Malcolm D, Barnett HAR. A mortality study of lead workers 1925–76. Br J Ind Med 1982;39:404–10.
17. McMichael AJ, Johnson HM. Long-term mortality profile of heavily-exposed lead smelter workers. J Occup Med 1982;24:375–8.
18. Davies JM. Long-term mortality study of chromate pigment workers who suffered lead poisoning. Br J Ind Med 1984;41:170–8.
19. DiPaolo JA, Nelson RL, Casto BC. *In vitro* neoplastic transformation of Syrian hamster cells by lead acetate and its relevance to environmental carcinogenesis. Br J Cancer 1978;38:452–5.
20. Boyland E, Dukes CE, Grover PL, et al. The induction of renal tumours by feeding lead acetate to rats. Br J Cancer 1962;16:283–8.
21. Zawirska B, Medras K. Tumoren und Storungen des Porphyrinstoff-Wechsels bei Ratten mit Chronischer Experimenteler Bleiintoxikation. I. Morphologische Studien. Zentralbl Allg Pathol 1968;111:1–12.
22. Van Esch GJ, Kroes R. The induction of renal tumours by feeding basic lead acetate to mice and hamsters. Br J Cancer 1969;23:765–71.
23. Van Esch GJ, Van Genderen H, Vink HH. The induction of renal tumours by feeding of basic lead acetate to rats. Br J Cancer 1962;16:289–97.
24. Mao P, Molnar JJ. The fine structure and histochemistry of lead-induced renal tumors in rats. Am J Pathol 1967;50:571–603.
25. Oyasu R, Battifora HA, Clasen RA, et al. Induction of cerebral gliomas in rats with dietary lead subacetate and 2-acetylaminofluorene. Cancer Res 1970;30:1248–61.
26. Baker EL, Goyer RA, Fowler BA, et al. Occupational lead exposure, nephropathy, and renal cancer. Am J Ind Med 1980;1:139–48.
27. Lilis R. Long-term occupational lead exposure, chronic nephropathy, and renal cancer: a case report. Am J Ind Med 1981;2:293–7.
28. National Institute for Occupational Safety and Health. Final report. Environmental phase, Bunker Hill Study. Prepared by ME Cassady, LB Larsen. Cincinnati, OH: National Institute for Occupational Safety and Health, 1975. Report no. 56.10.5.
29. National Institute for Occupational Safety and Health. An industrial hygiene survey of the zinc cell room, anode room, and zinc casting area: The Bunker Hill Company. Prepared by L Anderson, LB Larsen, W Spear. Cincinnati, OH: National Institute for Occupational Safety and Health, 1971. Report no. 56.10.
30. Johnson BL, Burg JR, Xintaras C, et al. A neurobehavioral examination of workers from a primary nonferrous smelter. Neurotoxicology 1980; 1:561–81.
31. Waxweiler R, Beaumont J, Henry J, et al. A modified life table analysis system for cohort studies. J Occup Med 1983;25:115–24.
32. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, DC: US GPO, 1979. (US DHHS (PHS, NIH), NIH publication no. 79-1649).
33. Breslow NE, Lubin JH, Marek P, et al. Multiplicative models and cohort analysis. J Am Stat Assoc 1983;78:1–12.
34. Yankel AJ, von Lindern IH, Walter SD. The Silver Valley lead study: the relationship of childhood lead poisoning and environmental exposure. J Air Pollut Control Assoc 1977;27:763–7.
35. Landrigan PJ, Baker EL Jr, Feldman RG, et al. Increased lead absorption with anemia and slowed nerve conduction in children near a lead smelter. J Pediatr 1976;89:904–10.
36. Emmerson BT. Chronic lead nephropathy. Kidney Int 1973;4:1–5.
37. Wedeen RP. Lead, mercury and cadmium nephropathy. Neurotoxicology 1983;4:134–46.
38. Cramer K, Goyer RA, Jagenburg R, et al. Renal ultrastructure, renal function, and parameters of lead toxicity in workers with different periods of lead exposure. Br J Ind Med 1974;31:113–21.
39. Malcolm D. The effects of lead on the kidney. Trans Soc Occup Med 1970;20:50–3.
40. Zollinger HU. Durch chronische Bleivergiftung erzeugte Nierenadenome und-Carcinoma bei Ratten und ihre Beziehungen zu den entsprechenden Neubildungen des Menschen. Virchows Arch (Pathol Anat) 1953;323:694–710.
41. Roe FJC, Boyland E, Dukes CE. Failure of testosterone or xanthopterin to influence the induction of renal neoplasms by lead in rats. Br J Cancer 1965;19:860–6.
42. Wagoner JK, Miller RW, Lundin FE, et al. Unusual cancer mortality among a group of underground metal miners. N Engl J Med 1963;269:284–9.
43. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976;30:225–30.
44. Beaumont JJ, Breslow NE. Power considerations in epidemiologic studies of vinyl chloride workers. Am J Epidemiol 1981;114:725–34.