MORTALITY STUDY OF LEAD WORKERS*

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The mortality of 7,032 men employed for one or more years in lead production facilities or battery plants was followed over a 23-year period, 1947—70. Lead absorption in many of these men was greatly in excess of currently accepted standards based upon urinary and blood lead concentrations available for a portion of the group. There were 1,356 deaths reported. The standardized mortality ratio (SMR) for all causes was 107 for smelter workers and 99 for battery plant workers. Death from neoplasms were in slight excess in smelters, but not significantly increased in battery plants. There were no excess deaths from kidney tumors. The SMR for cardiovascular-renal disease was 96 for smelter workers and 101 for battery plant workers. There was definitely no excess in deaths from either stroke or hypertensive heart disease; however, deaths classified as »other hypertensive disease« and »unspecified nephritis or renal sclerosis« were higher than expected. The life expectancy of lead workers was calculated to be approximately the same as that of all U. S. males.

One of the conclusions of an International Conference on Inorganic Lead, held in Amsterdam in November, 1968, to review permissible limits for inorganic lead in industry, was that »epidemiological study should be promoted, if possible on an international basis, on the effects of early, current, and past exposure, including long term sequelae, using tests for lead absorption of high specificity and sensitivity, and the most sensitive internationally accepted tests of biological change.« (1) The following year, the International Lead Zinc Research Organization, Inc. (ILZRO), began implementing plans for an epidemiologic study of lead

This study was sponsored and supported by the International Lead Zinc Research Organization, Inc., 292 Madison Avenue, New York 10017.

production workers and lead battery plant workers. Data obtained from members of ILZRO and from the Battery Council International showed that analysis of the mortality of a cohort of lead-exposed workers was feasible. Although it was recognized early that retrospective descriptions of individual lead absorption would be inadequate, it seemed feasible to develop a study population which could be grouped into those heavy, moderate and light exposures to lead.

In the initial plan, the goal was to obtain a total sample of about 12,000 individuals, 8,000 of whom would be available for epidemiologic study. It was also expected that two smelters and one battery plant outside the United States would be studied. For reasons to be discussed later, the latter studies (proposed in Australia, Belgium, and Japan) did not materialize.

DESCRIPTION OF STUDY

The investigation took the form of a prospective study of mortality in a sample of employees of United States lead production facilities and battery plants. The objectives were (1) to determine whether the pattern of mortality in male lead workers differed significantly from that which would have been expected in a similar population of males not occupationally exposed to lead; and (2) to determine if the patterns of mortality differed significantly with the date and length of employment, with the type of plant, with job titles, or with observed levels of blood and urine lead.

In early 1970, 101 U. S. plants and 28 non-U. S. plants, a total of 129 in all, had responded to a questionnaire asking if they were willing to participate in an epidemiologic study. The overwhelming majority, i. e. 108 with 36,000 current employees, responded affirmatively. Eventually 16 plants were included in the study. No attempt was made to get a truly representative sample. Self-selection had already occurred by membership in ILZRO and the Battery Council International and agreement to participate. The objective of the study was to learn whether or not workers in lead industries which had programs of industrial hygiene control showed long-term effects, and not to determine the incidence of lead toxicity *per se*. Selection of plants was based therefore upon their accessibility, their geographic distribution in the U. S., and the existence of adequate record systems. Unfortunately, it was not feasible to include plants outside the United States because of problems of followup and other operational problems associated with effective management from a California site.

In the six lead production facilities (loosely called »smelters« in the following report) and the ten battery plants which were selected for study, personnel records for 24,494 employees, employed during the period January 1, 1946 through December 31, 1970, were microfilmed by

TCA staff members. After elimination of female employees (mainly clerical), men who worked for less than one year, and about 350 others with grossly deficient records, a study population of 7,032 men remained.

Serial data on urinary lead and blood lead determinations were obtained from nine plants.

Followup to determine vital status was carried out by the usual methods, i. e. plant personnel records, telephone directories, postal inquires, drivers' license bureaus, retail credit bureaus, and (for all but two plants) review of records by the Social Security Administration.

Causes of death for decedents were coded from death certificates applying the rules in the Seventh (1955) Revision of the International Classification of Diseases, Injuries and Causes of Death. The coding was done under the close supervision of two former employees of the California State Department of Public Health.

The specific causes were grouped into a summary list consisting of the standard 35-cause list used in national statistics (minus breast cancer and diseases of the newborn) plus some causal groups related to infectious disease and to renal disease.

Proportionate mortality for 12 selected causes was compared with the distribution for United States male deaths in 1959.

Standardized mortality ratios (SMR's) were calculated, in which the ratio of observed to expected deaths was determined taking into consideration the age of the study population during the time periods of observation. For this purpose, each man was considered as coming under observation one year after Januay 1, 1946, or one year after his hire date if that was after January 1, 1946. The calculation of expected deaths required that the number of years of observation be computed for each worker and classified by the years of age over which he was followed, and his date of birth. Cause-specific death rates were applied to the number of person years observed for each 5-year age period. Statistical significance was determined by first calculating the standard error of each SMR, using the technique described by *Chin Long Chiang*, (2) i. e.

$$SE = \sqrt{\frac{100 \times SMR}{\text{expected deaths}}}$$ If an observed SMR differed from 100 by more than 1.96 standard errors, it was interpreted as significant at the 5% level, if more than 2.57 standard errors at the 1% level. This formula is slightly conservative and of doubtful applicability for very small numbers. Significance was not tested when SMR's were based on fewer than five deaths.

Calculations of life expectancy were also carried out by the method of *Chin Long Chiang* (3), comparisons being made with corresponding figures for U. S. males in 1949—51, 1959—61 and 1969.

RESULTS

Characteristics of study population. Table 1 shows the distribution of the study population by year of hire. Of the battery plant workers, 2,588 (55.3%) had been hired before 1945, while only 456, or 19.4%, of smelter workers had hire dates this early. Actual entry into the study for mortality analysis was January 1, 1947 for those hired before 1946 and one year after the date of hiring for those employed after January 1, 1946.

Table 1

Distribution of smelter and battery workers by year of hire

Year hired	Totals	Smelter workers	Battery workers
1900—04	6	1	5
1905—09	16	4	12
1910—14	63	11	52
1915—19	243	18	225
1920—24	494	59	435
1925—29	412	65	347
1930—34	135	51	84
1935—39	294	85	209
1940—44	1381	162	1219
1945—49	925	503	422
1950—54	792	511	281
1955—59	482	225	257
1960—64	684	295	389
1965—69	1105	362	743
Total	7032	2352	4680

Table 2 summarizes the distribution of the study population by age at time of entry into the mortality study. Smelter workers tended to be somewhat younger than battery plant workers, although 16.5% of the former and 25.8% of the latter were 45 years of age or older at the time observation was begun.

Table 3 shows the distribution of length of employment of the study group, i. e. the intervals from date of hiring to the date of termination or to December 31, 1970 whichever came first. Battery workers tended to have longer work histories than smelter workers.

It was impossible to obtain precise information on racial distribution from personnel records. Seven plants which accounted for 80 percent of

Table 2

Distribution by age at entry into study for smelter and battery workers

Age at entry	Totals	Smelters		Battery	
		Number	Percent	Number	Percent
	7032	2352	100	4680	100
Under 25	1480	630	26.8	850	18.2
25—34	2422	801	34.0	1621	34.6
35—44	1524	529	22.5	995	21.3
45—54	1027	271	11.5	756	16.1
55—64	497	118	5.0	379	8.1
65—74	82	3	0.1	79	1.7

Table 3

*Distribution by number of years employed** for smelter and battery workers*

Years employed	Totals	Smelters		Battery	
		Number	Percent	Number	Percent
	7032	2352	100.0	4680	100.0
1— 5	2493	1082	46.0	1411	30.1
6—10	1131	338	14.4	793	16.9
11—15	747	187	7.9	560	11.9
16—20	458	182	7.7	276	5.9
21—25	479	204	8.7	275	5.9
26—30	613	139	5.9	474	10.1
31—35	518	88	3.7	430	9.2
36—40	311	63	2.7	248	5.3
41—45	138	34	1.4	104	2.2
46—50	28	6	.3	22	.5
51*	1	1	—	—	—
Unknown*	115	28	1.2	87	1.8

* Date of termination of these workers was undetermined.
** As of date of termination or December 31, 1970, whichever came first.

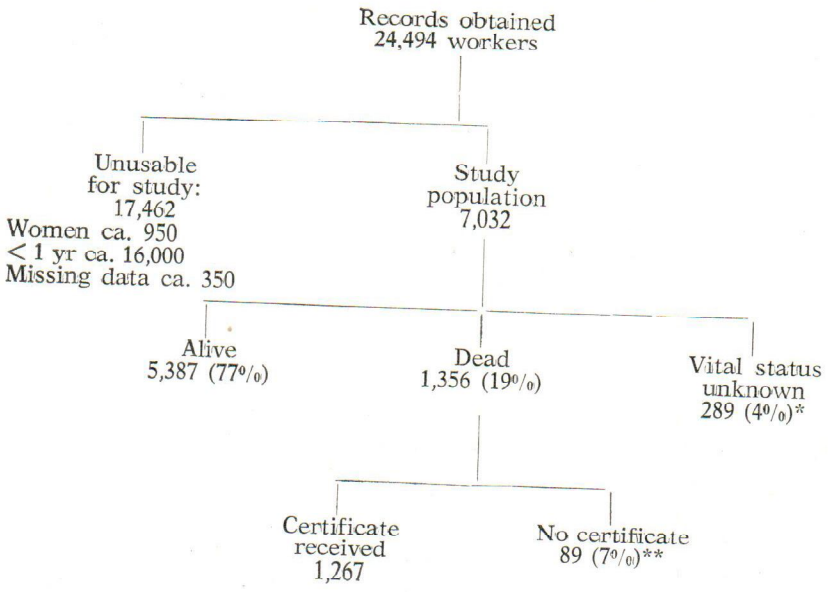
the smelter workers in the study and 71 percent of the battery plant workers, were able to provide estimates of the racial distribution during the 1960's. The estimated percent non-white was 25 percent for smelters and 10 percent for battery plants. Although these figures are only rough estimates of the proportion of person-years contributed by whites and

non-whites, it appears that the battery plant group had approximately the same proportion of non-whites as the general population (11%), while non-whites were substantially overrepresented among the smelter workers.

Followup. Results of followup are summarized in Tables 4, 5, and 6. Plants are numbered in the order in which they were visited. Vital status was determined for 96% of the study population, representing 98% of smelter workers and 95% of battery plant employees. The failure rate was not evenly spread over the 16 plants, but largely represented poor results in battery plants 16 and 17. These were the last ones visited and data on missing workers were not included in the Social Security followup. For battery plants other than these two, the followup percent was approximately 99%.

There were 1,356 individuals known to have died; death certificates were obtained for 1,267 or 93%. This represented about 92.0% in battery plants and 94.5% in smelters. In calculations of standardized mortality ratios, appropriate corrections have been made on the assumption that distribution of causes of death was the same in missing certificates as in those that were obtained.

Table 4



* 193 of these from 2 smaller plants where no Social Security followup
** 70 from one plant in Pennsylvania

Table 5

Battery plant study population by plants with per cent follow-up

Plant code	Number in study group	Per cent located
2	338	99
5	106	97
7	2834	99
9	113	100
10	334	99
12	97	96
13	221	97
14	168	98
16	271	68
17	198	46
Total	4680	95
Less 16 & 17	4211	99

Table 6

Production facility (»smelter«) study population by plants with per cent follow-up

Plant code	Number in study group	Per cent located
1	96	100
4	111	99
6	811	99
8	364	93
11	533	99
15	437	99
Total	2352	98

Biological data on lead absorption. Fifteen of the 16 plants in the study were carrying out programs of biologic monitoring as of 1970, and we obtained detailed records from nine (Table 7). Because the plants had begun their programs at different times during the study period (1946—1970), many workers had no recorded urinary or blood lead values, their entire work experience having been before such monitoring began.

Table 7

Summary of urinary and blood lead determinations

Type of plant	No. in study	No. with samples	% sampled	Total No. samples	Samples/ man
Urine					
Battery	4680	1286	27.5%	85,065	66.1
Smelter	2352	989	42.0%	12,140	12.3
Total	7032	2275	32.4%	97,205	42.7
Blood					
Battery	4680	1325	28.3%	14,040	10.6
Smelter	2352	537	22.8%	2,370	4.4
Total	7032	1863	26.5%	16,410	8.8

Of the 7,032 workers in the study 2,768 worked during periods when their particular plants monitored urine for lead. We obtained data for 2,275. This represented only 32.4% of the men in the entire study. PbU figures were available for nearly all of the 997 active employees, but for only less than half of the terminated employees. Urinary lead values were available for only 132 (9.7%) of the 1,356 deceased workers.

There were similar limitations in blood lead values. Of the 7,032 individuals in the study population, 2,060 worked during periods when their plants monitored blood for lead. PbB values were obtained for 1,863. Here again, representation among active workers was high; but it was relatively low for terminated workers, and only 23 of the 1,356 deaths (less than 2%) were in individuals for whom there was information on blood lead.

Table 8 summarizes urinary lead values in 6 battery plants and three smelters. The mean of all determinations for each worker was first determined, then an average of these means was calculated, as well as the number of worker-means exceeding specified concentrations. The proportion of individuals with high mean values in part reflected company policy as to who would sampled. If a program concentrated on areas where lead exposures were potentially high, a relatively large proportion of individuals would be expected to show high lead values. On the other hand, if all employees monitored, the percentage naturally would be lower. The absolute numbers of individuals whose mean PbU concentrations exceeded 150 μg/liter or 200 μg/liter over a period of years is striking.

Table 8

Summary of urinary lead concentrations in 6 battery plants and 3 smelters (uncorrected for specific gravity)

Type of plant	Total number of workers sampled	Analysis of data for men with 10 or more samples						
		No.	Average samples/man	Average of worker-means μg/liter	Number of worker-means equal to or greater than			
					150	200	250	300 μg/L
Battery	1286	1053	80.2	129.7	249	59	17	7
Smelter	989	497	20.0	173.2	289	164	70	27
Total	2275	1550	60.9	142.9	538	223	87	34

Similar information for blood lead values is summarized in Table 9. The average of the worker-means, and the proportion of worker-means exceeding 40 μg/100 g or 80 μg/100 g is even more dependent upon company policy than in the case of PbU values. Values are strongly influenced by whether or not all employees are included, or only those with potential high lead exposures, and also by whether or not blood sampling is done only when an elevated PbU has been reported. For this reason the worker-means and percentages are artificially elevated and do not

Table 9

Summary of blood lead concentrations for workers in 6 battery plants and 4 smelters

Type of plant	Total number of workers sampled	Analysis of data for men with 3 or more samples						
		No.	Average samples/man	Average of worker-means μg/100 g	Number of worker means equal to or greater than			
					40	70	80	100 μg/100 g
Battery	1326	1083	12.6	62.7	1009	278	102	24
Smelter	537	254	7.6	79.7	241	89	56	18
Total	1863	1337	11.7	64.0	1250	367	158	42

necessarily represent industry averages. Nevertheless, the absolute numbers of workers with long-term mean PbB values above 80 μg/100 g is important to consider in interpretation of the data on mortality.

Correlation between urinary and blood lead values and mortality was impossible, because data were not available for many workers and because the distribution between active, terminated, and deceased employees was markedly uneven.

Tables 10 and 11 illustrate the correlation between mean urinary and blood lead concentrations and exposure categories based upon last job title. They corroborate the estimation of relative exposures by industrial hygienists, but also show that even the low exposure categories represented appreciable levels of lead absorption.

Table 10

Urinary lead concentrations (uncorrected for specific gravity). Means of all recorded values for individuals classified for probable lead exposures on basis of last job title

Type of plant and group	Urinary lead concentrations, μg/liter Exposure category		
	High	Medium	Low
Battery			
Entire study period	153	129	105
Period 1965—70	157	131	107
Smelter			
Entire study period	182	165	130
Period 1965—70	165	146	111

Table 11

Blood lead concentrations. Average worker-means for individuals classified by probable lead exposures on basis of last job title

Type of plant and group	Urinary lead concentrations, μg/liter Exposure category		
	High	Medium	Low
Battery			
Entire study period	64	59	55
Period 1961 et seq.	65	69	54
Smelter			
Entire study period	60	62	49
Period 1961 et seq.	59	61	49

Proportionate mortality. The distribution of certified deaths in the study population for 12 selected causes is shown in Table 12, compared with the distribution of United States male deaths in 1959. There are suggestive discrepancies for »malignant neoplasms«, »other hypertensive disease« and for »chronic and unspecified nephritis.« Stroke, i. e. vascular lesions of the CNS, was not disproportionately high.

Table 12

Percentages of 1267 death in smelter and battery workers due to selected causes, compared with percentages among U. S. males for 1959 (proportionate mortality)

Cause of death	U. S. Males	Smelter Workers	Battery Workers
Major cardiovascular, renal diseases (330—334, 400—468, 592—594)	53.9	45.7	57.3
Vascular lesions of CNS (330—334)	9.7	7.4	7.1
Hypertensive heart disease (440—443)	3.2	3.1	3.1
Other hypertensive disease (444—447)	0.7	2.2	1.4
Chronic and unspecified nephritis (592—594)	0.7	2.2	1.5
Malignant neoplasms (140—205)	14.6	21.3	19.7
Malignant neoplasms of respiratory system (160—164)	3.4	6.8	6.5
Malignant neoplasms of urinary organs (180, 181)	0.9	1.5	0.5
Cirrhosis of liver (581)	1.3	0.6	2.8
Suicide (963, 970—979)	1.5	4.0	1.7
Motor vehicle accidents (810—835)	3.0	4.6	1.9
Other	25.7	23.8	16.6

Standardized mortality rations. Table 13 presents standardized mortality ratios for the study populations in smelters and battery plants. Two SMR's were significantly high, that for malignant neoplasms and that for violent deaths in smelter workers. The SMR for violent deaths was significantly lower in battery plants.

Table 13

Expected and observed deaths by cause Jan. 1, 1947 — Dec. 31, 1970 for lead smelter and battery plant workers

Cause of death	Smelters			Battery plants		
	Obs	Exp	SMR*	Obs	Exp	SMR**
Tuberculosis, all forms	1	4.55	23	5	14.84	37
Bacterial and viral diseases plus influenza and pneumonia	8	8.17	103	23	26.82	92
Malignant neoplasms	69	54.95	133	186	180.34	111
Major cardiovascular renal disease	151	165.29	96	540	575.21	101
Violent deaths	59	40.52	154	62	89.63	74
All other certified causes	36	46.15	82	127	141.45	97
Total for certified causes	324	319.64	107	943	1028.37	99
All causes including uncertified	342	319.64		1014	1028.37	
Number of workers		2352			4680	
Person-years		33482			69828	

* Correction of + 5.55% aplied for 18 missing death certificates
** Correction of + 7.52% applied for 71 missing death certificates

Table 14 examines in greater detail the distribution of malignant neoplasms found in the population. Slight but not statistically significant excesses are found for digestive organs and the respiratory system in both smelter workers and battery plant workers.

The 69 deaths in smelter workers and 186 deaths in battery workers attributed to malignant neoplasms were subjected to more detailed scrutiny to determine if there were any unusual features, either of anatomical site or of exposure, which might suggest causative relationships. Primary smelters showed no excess of tumor deaths when compared with secondary smelters and refineries. There were no rare or unexpected tumors found. Tumors of the respiratory tract were predominantly bronchogenic carcinoma, and there was no unusual distribution of sites within the gastrointestinal tract. Tumors of the urinary tract were distributed as shown in Table 15; only three primary tumors of the kidney were diagnosed. There were also seven tumors of the central nervous system (Table 16), a number consistent with the expected proportion in 255 malignant neoplasms. Analyses by site, based on duration of employment, date of hire, or estimated lead exposures showed no consistent relationships.

Table 14

Expected and observed deaths for malignant neoplasms
Jan. 1, 1947 — Dec. 31, 1970
Lead smelter and battery plant workers

Cause of death	Smelters			Battery plants		
	Obs	Exp	SMR*	Obs	Exp	SMR**
All malignant neoplasms (140—205)	69	54.95	133	186	180.34	111
Buccal cavity & pharynx (140—148)	0	1.89	—	6	6.02	107
Digestive organs, peritoneum (150—159)	25	17.63	150	70	61.48	123
Respiratory system (160—164)	22	15.76	148	61	49.51	132
Genital organs (170—179)	4	4.15	101	8	18.57	46
Urinary organs (180—181)	5	2.95	179	5	10.33	52
Leukemia (204)	2	2.40	88	6	7.30	88
Lymphosarcoma, lymphatic and hematopoietic (200—203, 205)	3	3.46	92	7	9.74	77
Other sites	8	6.71	126	23	17.39	142

* Correction of + 5.55% applied for 18 missing death certificates
** Correction of + 7.52% applied for 71 missing death certificates

Table 15

Urinary tract neoplasms
(diagnoses from death certificates)

Lead production facilities (342 total deaths, 69 cancer deaths)
- Hypernephroma with metastasis to spine (Autopsy)
- Malignant tumor of left kidney (No Autopsy)
- Primary adenocarcinoma of the bladder (No Autopsy)
- Carcinomatosis of urinary bladder (No Autopsy)
- Carcinoma of urethra (No Autopsy)

Battery plants (1,014 total deaths, 186 cancer deaths)
- Metastatic renal adenocarcinoma (Autopsy)
- Carcinoma of urinary bladder (Autopsy)
- Carcinoma, bladder (Autopsy)
- Anaplastic carcinoma bladder with metastasis to neck (Autopsy?)
- Carcinoma of the urinary bladder (Autopsy)

Summary: Kidney 3
Bladder 6
Urethra 1

Table 16

Tumors of the central nervous system (diagnoses on death certificates)

Lead production facilities (342 total deaths, 69 cancer deaths)
- Glioblastoma multiforme of frontal lobe of cerebral cortex (No Autopsy)
- Malignant brain tumor (No Autopsy)
- Glioma (Autopsy)
- Astrocytoma (Autopsy)

Lead battery plants (1,014 total deaths, 186 cancer deaths)
- Glioblastoma multiforme (No Autopsy)
- Malignant brain tumor (Autopsy)
- Glioma left temple (No Autopsy)

Table 17 summarizes observed and expected deaths for major cardiovascular and renal diseases in the two groups. Overall SMR's after correction for missing death certificates were approximately the same as for the general U. S. male population. Of particular interest is the lack

Table 17

Expected and observed deaths for major cardiovascular and renal disease Jan. 1, 1947 — Dec. 31, 1970 for lead smelter and battery plant workers

Cause of death with ICD No	Smelters			Battery plants		
	Obs	Exp	SMR*	Obs	Exp	SMR**
Major cardiovascular and renal disease (330—334, 400—468, 592—594)	151	165.29	96	540	575.21	101
Vascular lesions affecting CNS (330—34)	24	23.23	109	67	87.93	82
Arteriosclerotic heart disease (420)	77	104.95	77	340	355.70	103
Hypertensive heart disease (440—443)	10	8.72	121	29	32.30	97
Other hypertensive disease (444—447)	7	1.90	389	13	6.26	223
Chronic & unspecified nephritis (592—594)	7	2.80	264	14	8.58	175
Rheumatic heart disease; endocarditis	12	11.12	114	42	37.80	119
Other	14	12.57	118	35	46.64	81

* Correction of + 5.55% applied for 18 missing death certificates
** Correction of + 7.52% applied for 71 missing death certificates

of excess deaths from vascular lesion affecting the central nervous system (i. e. stroke), arteriosclerotic heart disease, and hypertensive heart disease. There is, however, a consistent pattern of increase in »other hypertensive disease«, and »for chronic nephritis, nephritis not specified as acute or chronic and other renal sclerosis«. SMR's for each of these is at the borderline of significance at the 5% level, even though the actual numbers of deaths were small.

Further analysis of the 41 individuals whose deaths were attributed to the above causes was not informative. The average age at death was 57.2 years and the average length of service in the lead industry was 24.2 years. Nine of the 41 were black and 32 Caucasian. Autopsies were known to have been performed in only 15 of the 41 cases. Review of medical records provided relatively little useful information; there were too few records of blood pressure readings, urinalyses or clinical observations to make analysis worthwhile. It should be emphasized that much of this study dealt with records dating back 25 or 30 years. The illnesses of a large proportion of those who died occurred after termination of employment, and it was not feasible to track down all medical observations by their private physicians.

A separate analysis was made of the observed and expected deaths by cause for the smelter workers and battery plant workers hired before January 1, 1946. These totalled 3,130 individuals observed for 60,883 per-

Table 18

Observed and expected deaths by cause
Jan. 1, 1947 — Dec. 31, 1970
for lead smelter and battery plant workers
hired before Jan. 1, 1946

Cause of death	Smelters			Battery plants		
	Obs	Exp	SMR*	Obs	Exp	SMR**
Tuberculosis, all forms	1	2.55	40	5	13.71	39
Bacterial and viral diseases plus influenza and pneumonia	5	4.50	115	22	24.65	96
Malignant neoplasms	42	30.80	140	172	167.29	111
Major cardiovascular renal disease	103	99.24	107	521	540.49	103
Violent deaths	16	12.26	135	45	68.55	71
All other certified causes	20	23.47	88	120	127.98	101
Total for certified causes	187	172.96	112	885	942.75	101
Total, including uncertified	193	172.96		954	942.75	
Number of workers		491			2639	
Person-years		9232			51651	

* Correction of + 3.2% applied for 6 missing death certificates
** Correction of + 7.8% applied for 69 missing death certificates

son-years between January 1, 1947 and December 31, 1970, during which time they experienced 1,147 deaths. As shown in Table 18, restriction of analysis to this population did not significantly affect the results.

Workers included in the study population were, on the basis of their last designated jobs, classified as having had high, medium, or low levels of lead exposure. In the smelters, 509 men were classified as in the high group, 391 in the medium group and 556 in the low group, while for 815 the category was unknown. In the battery plants, classification into high, medium, low, and unknown were 840, 1875, 1168 and 707 men respectively. Attempts to relate standardized mortality ratios by cause to this classification produced no consistent results. This was attributed to the imprecision of relating job to exposure, changes in job title during work experience and to the relatively small numbers of deaths in various categories after this fragmentation, in the absence of any overriding cause-and-effect relationships.

Because 3,645 (52%) of the 7,032 workers in the study came from plants in the state of Pennsylvania, and since this group contributed 1,005 (74%) of the deaths in the study, a special analysis was carried out to determine if this geographic overrepresentation had biassed the study. Calculation of standardized mortality ratios using Pennsylvania rate figures as a standard caused no substantive change in the results.

Life expectancy. A calculation of the life expectancy of smelter and battery plant workers was made, based on the method of *Chin Long Chiang* (3). The calculation answers the following question: if a man alive at age 20 is subjected, at each subsequent period of his life, to the same mortality as was observed among lead workers in this study, at what age can he expect to die?

The calculated figure for smelter workers was 69.7 years and that for battery plant workers 71.5 years (Table 19). The corresponding figures for U. S. males in 1949—1951 was 68.9 years, that for 1959—61 was 69.8 years.

Table 19

Expected age at death after age 20

Smelter workers	69.7*
Battery plant workers	71.5*
U. S. males 1949—51	68.9
U. S. males 1959—61	69.8
U. S. white males 1969	70.1
U. S. non-white males 1969	63.9
(Steel workers	72.6)**

* Method of Chiang (3)

** Calculated from data of Lloyd & Ciocco (6)

DISCUSSION

Overall mortality. The standardized mortality ratio of smelter workers and battery plant workers combined was 101, indicating that the total number of deaths was approximately that expected in the years 1947 to 1970 in a male population of this age distribution. The SMR for smelter workers was 107 and that for battery plant workers 99.

This is not a highly favorable finding, as most employed populations show SMR's below 100, unless there is some over-riding adverse factor. (4, 5). This has been explained by the early selection out of the work force of many individuals with life-shortening conditions and possibly by other favorable factors associated with employment. Examples of such favorable SMR's include that of 82 for steelworkers (6) and 88 for cotton textile workers (7). On the other hand, groups with strongly operating health hazards such as underground uranium miners, asbestos insulation workers, and asbestos maintenance workers show distinctly unfavorable SMR's.

Since it was estimated that 25% of the smelter workers were non-white, compared with 11% in the general population, and since non-whites experience a total age-corrected mortality about 30% greater than whites, one might speculate that the observed overall SMR for smelter workers was inflated by about 4%. This is not a fully justified correction however in view of inability to correct for economic and geographic factors. The racial distribution is probably of more importance when one considers certain cause-specified rates.

Malignant neoplasms. The standardized mortality ratio for all malignant neoplasms was slightly elevated, at the 5% confidence level for smelter workers but was not significantly elevated for battery plant employees. Although there were small excesses in tumors of the digestive organs and the respiratory systems, these were not statistically significant deviations.

The absence of renal tumors is of interest in view of the experimental production by a number of investigators of renal adenomas or adenocarcinomas in rats and mice by the oral or parenteral introduction of lead salts (8). *Dingwall-Fordyce* and *Lane* (9) in 1963 concluded from a study of pensioned battery plant workers that there was no evidence for an association between lead exposures and malignant disease. While our study does not support an association between lead *per se* and tumors, there is a strong suggestion that there is a slightly increased risk of respiratory tract and gastrointestinal tract tumors in lead production facilities. Continued observation is recommended.

Bacterial and viral diseases, plus influeza and pneumonia. Although this is not a standardized grouping commonly employed in mortality analyses, these causes of death were combined in view of the suggestion by some investigators, that lead had an adverse effect on immune responses. There was no evidence of increased risk of death from these groups of infectious diseases among the lead workers we studied.

Major cardiovascular and renal disease. Overall standardized mortality ratios for major cardiovascular and renal disease were essentially the same as that in the general population. Such SMR's are not quite as favorable as would be expected in a study that began with a working population, but do not indicate any major risk associated with working in lead smelter or battery plants.

Vascular lesions affecting the central nervous system. There was no excess of deaths from causes included under the common heading of »stroke«. This is not in agreement with earlier reports suggesting that heavy lead exposures were associated with cerebrovascular accidents. *Dingwall-Fordyce* and *Lane* (9) reported a study of 425 pensioners who had worked in lead battery plants. Of these, 187 were men who were regarded as having had heavy lead exposures, as demonstrated by mean PbU values between 100 and 250 µg/l over a 20-year period, with even higher values before that. Overall deaths were 184 compared with 167.1 expected, with the major excess in the heavily exposed group, where there were 24 deaths due to cerebral hemorrhage, cerebral thrombosis and cerebral arteriosclerosis instead of the 9.3 expected. *Lane* (10) later reported on the same group and while there was no excess in »all diseases of the circulatory system« (35 vs 37.4 expected), vascular lesions of the central nervous system accounted for 29 deaths where 12.6 were expected. His less-heavily exposed workers did not show such an excess. Our data do not indicate that death from stroke represents an unusual threat to U. S. smelter and battery plant workers.

Hypertensive heart disease is similarly not in significant excess in our series, the SMR for smelter workers being 121 and that for battery plant workers 97. Racial differences in mortality from this cause are such that the observed SMR in smelters can in part be explained by the fact that the workforce is probably about 25% non-white. This failure to show excessive deaths from hypertensive heart disease is consistent with a number of clinical studies, which have failed to show excessive incidence of arterial hypertension in workers exposed to lead (11—16).

Other hypertensive disease and chronic nephritis, unspecified nephritis and renal sclerosis. In contrast with the foregoing, there were elevated SMR's for both smelter workers and battery plant workers in these categories. Review of the actual diagnoses reported on the 20 death certificates classified as other hypertensive disease shows that in 17 there was specific mention of uremia, nephrosclerosis or other renal disease. This excess, although of marginal statistical significance in view of the small numbers involved, is consistent with other evidence relating lead to renal damage.

A number of early clinical reports describe an association between lead and kidney disease (17—21). There are studies of renal function in individuals subsequent to episodes of severe lead poisoning which have shown impaired function and some such individuals have exhibited chronic renal failure (22–24). *Lane* (10) described nine deaths from chronic azotemic nephritis in a group of about 150 men who had worked

for over 20 years in areas of high airborne lead (above 500 μg/cubic meter). While *Henderson* (25) and *Henderson* and *Inglis* (26) reported that childhood plumbism was followed by a high incidence of chronic renal disease, *Tepper* (27) was unable to confirm this when he traced 139 individuals who had had childhood plumbism in the United States.

Despite the uncertainties of diagnosis inherent in death certificates, the excess of deaths in our study from »other hypertensive disease« and »chronic nephritis or other renal sclerosis« supports the view that high levels of lead absorption such as occurred in many of workers in this series may be associated with chronic renal disease. More detailed study of the 41 cases in these categories, however, yielded no meaningful association with job titles, duration of exposure, or clinical data.

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Sažetak

PROUČAVANJE MORTALITETA U RADNIKA IZ INDUSTRIJE OLOVA

U opsežnom epidemiološkom istraživanju mortaliteta u radnika koji su radili više od godinu dana u topionicama olova ili u proizvodnji akumulatora obuhvaćena su 7032 muškarca, i to u razdoblju od 23 godine (1947. do 1970). Svrha je ovog istraživanja bila utvrditi da li je mortalitet u ovih radnika drugačiji od onog što se može očekivati u sličnoj populaciji muškaraca koji nisu eksponirani olovu. Osim toga željelo se utvrditi da li postoje razlike u mortalitetu s obzirom na razinu olova u krvi i mokraći. Nije prema tome bila svrha proučavati učestalost pojedinih štetnih učinaka olova već saznati da li se u spomenutih radnika javljaju ikakvi kasni učinci koji bi bili uzrokom drugačijeg mortaliteta.

Uzroci su smrti grupirani u zbirnu listu prema Međunarodnoj klasifikaciji bolesti, ozljeda i uzroka smrti. Od 1356 umrlih bivših radnika, podaci o uzroku smrti utvrđeni su u 93% slučajeva. Podaci o olovu u mokraći postojali su za gotovo sve radnike koji su bili aktivni u vrijeme ovih istraživanja, ali samo za 2% umrlih radnika, tako da su analizirani podaci samo od 2275 radnika. Kompilirani su i podaci o koncentraciji olova u krvi, ali zbog nedostatka podataka za mnoge radnike i zbog nejednolike razdiobe ovih podataka između aktivnih i bivših radnika nisu se mogle korelirati vrijednosti olova u mokraći i krvi s mortalitetom.

Ukupna smrtnost u radnika iz industrije olova nije se bitno razlikovala od one u općoj populaciji. Izračunato očekivano trajanje života za ovu skupinu radnika (u 20. godini života) iznosi 69.7 godina (za radnike iz topionica) odnosno 71.5 godina (za radnike iz proizvodnje akumulatora). Te se vrijednosti ne razlikuju bitno od očekivanog trajanja života prosječnog dvadesetogodišnjeg američkog muškarca (69.8 godina).

Smrtnost od neoplazmi u radnika iz topionica bila je neznatno veća od one što se računski moglo očekivati, ali u ukupnom broju smrtnost je bila tek granično statistički značajno veća. Nije bilo rijetkih neoplazmi ili onih neobične lokalizacije. Valja spomenuti da nije bilo bubrežnih tumora. Smrtnost od srčanih i bubrežnih bolesti također se nije razlikovala prema općoj populaciji. Malena, ali statistički značajna razlika utvrđena je u uzrocima smrti od kroničnog nefritisa i drugih bubrežnih bolesti. Taj je nalaz u suglasnosti s rezultatima proučavanja učinaka olova na pokusnim životinjama.

Uzimajući u obzir razine ekspozicije i ponešto veći mortalitet u nekim kategorijama, može se zaključiti da odrasli muškarci, bijelci, eksponirani olovu u granicama postojećih standarda, vjerojatno neće pokazati značajnih razlika u mortalitetu u odnosu na neeksponirane ljude.