

Deaths from Chronic Renal Disease in U.S. Battery and Lead Production Workers

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This report is based on an analysis of deaths in 4519 battery plant workers and 2300 lead production or smelter workers during the years 1947 to 1980. Causes were coded to the seventh (1955) revision of the International Classification of Diseases. There were significant excess deaths for "other hypertensive disease" (444-447) and "chronic nephritis" (592-594) in both cohorts, the standardized mortality ratios (SMRs) being 320 and 475, respectively, for the former causes and 222 and 265 for the latter. Proportionate mortality analysis, which adjusted for race, also showed elevated ratios, 241 and 388 for the former causes and 296 and 186 for the latter. Deaths from other hypertension-related diseases did not show comparable excesses. Renal cancer deaths were fewer than expected, SMRs being 41 and 74, respectively.

Description of Study

Deaths during the years 1947 to 1980 were studied in two cohorts of lead workers (1,2). The first consisted of 4519 workers from 10 U.S. battery plants who had been employed for at least 1 year and who had worked between January 1, 1946 and December 31, 1970. The second cohort was 2300 workers from six lead production plants or smelters (1 primary smelter, 2 refineries, and 3 secondary smelters), with similar work criteria.

Follow-up through 12/31/80 accounted for 94.7% of the battery workers and 91.6% of the smelter workers. There were 1636 certified deaths in the former and 579 in the latter cohort. Standardized mortality ratios (SMRs), with U.S. white male deaths used for comparison, were calculated using the Occupational Cohort Mortality Analysis Program (3). For some causes of major interest, detailed computer programs were unavailable, so hand calculations were needed. Deaths were coded to the seventh (1955) revision of the International Classification of Diseases (ICD) (4).

Classifications of Renal Disease

The categories of chronic disease were those which appear in the seventh ICD revision under the categories of "other hypertensive disease" (rubrics 444-447), and "chronic nephritis" (592-594). The former category includes essential benign hypertension (444),

essential malignant hypertension (445), hypertension with nephrosclerosis (446), and other hypertensive disease without mention of heart (447). These correspond to malignant hypertension (400), essential benign hypertension (401), and hypertensive renal disease (403) in the eighth or 1965 revision (5). The chronic nephritis classification (592-594) excludes acute nephritis and nephrosis, but includes chronic nephritis (592), nephritis not specified as acute or chronic (593), and other renal sclerosis (594). These correspond to chronic nephritis (582), nephritis unqualified (583), and renal sclerosis unqualified (584) in the eighth revision.

Mortality Ratios

Table 1 shows the observed and expected deaths for the foregoing causes; all SMRs were significantly elevated.

Table 1. Standard mortality ratios in lead worker cohorts.

Causes ^a	Battery		Smelter	
	O/E	SMR	O/E	SMR
Other hypertensive disease (444-447)	21/6.6	320 [†]	9/1.9	475 [†]
Chronic nephritis (592-594)	20/9.0	222 [*]	8/3.0	265 [*]

^aICD, seventh revision, 1955.

^{*}Statistically significant, $p < 0.05$.

[†]Statistically significant, $p < 0.01$.

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Death rates from hypertension-related diseases are higher in blacks than in whites. Proportionate mortality ratios (PMRs) were calculated (Table 2), as these permit adjustment for race; 6.6% of battery deaths and 25% of smelter deaths were in black workers. The expected numbers are those that would have occurred if the proportions of total deaths due to those specific causes had been the same as in the U.S. male deaths for the same time period, adjusted for age and whether white or nonwhite. It can be seen that PMRs were somewhat lower than SMRs. Nevertheless, PMRs were significantly elevated in all but one comparison.

Deaths from Other Hypertension-Related Diseases

Several other causes of death associated with elevated blood pressure were investigated. These include hypertensive heart disease and cerebrovascular disease (Table 3). The only SMR that was significantly elevated was that for hypertensive heart disease in smelter workers; however, proportionate mortality analysis (Table 4) suggested that the elevations were largely explained by race.

Six of the 35 deaths coded to hypertensive heart disease in battery workers were coded to rubric 442, hypertensive heart disease with arteriolar nephrosclerosis, corresponding to rubric 404 in the eighth revision (hypertensive heart and renal disease).

There were no excess deaths from cancer of the kidney, i.e., 3 with 7.3 expected in battery workers (SMR = 41) and 2 with 2.7 expected in smelter workers (SMR = 74).

Table 2. Proportionate mortality ratios in lead workers.

Causes ^a	Battery		Smelter	
	O/E	PMR	O/E	PMR
Other hypertensive disease (444-447)	21/8.7	241 [†]	9/2.3	388 [†]
Chronic nephritis (592-594)	20/9.7	206 [*]	8/4.3	186

^aICD, seventh revision, 1955.

^{*}Statistically significant, $p < 0.05$.

[†]Statistically significant, $p < 0.01$.

Table 3. Standard mortality ratios for hypertension-related disease in lead workers.

Causes ^a	Battery		Smelter	
	O/E	SMR	O/E	SMR
Vascular disease of CNS (330-334)	122/131.6	93	50/37.8	132
Hypertensive heart disease (440-443)	35/27.4	128	15/7.4	203 [*]

^aICD, seventh revision, 1955.

^{*}Statistically significant, $p < 0.05$.

Table 4. Proportionate mortality ratios for hypertension-related disease in lead workers.

Causes ^a	Battery		Smelter	
	O/E	PMR	O/E	PMR
Vascular disease of CNS (330-334)	122/149.4	82 [*]	50/48.1	104
Hypertensive heart disease (440-443)	35/32.3	109	15/11.7	128

^aICD, seventh revision, 1955.

^{*}Statistically significant, $p < 0.05$.

Relation to Lead Exposures

It was not possible to divide the population into sub-cohorts with estimated levels of lead exposure during different portions of their work histories. Blood lead and urine lead determinations during varying time periods between 1947 and 1972 are available for about 30% of the populations. These document high exposures, even after monitoring had been instituted, with many men having average urine lead levels greater than 100 $\mu\text{g/L}$ and blood lead concentrations greater than 70 $\mu\text{g/dL}$.

Discussion

Numbers of deaths from chronic renal disease were significantly higher than expected in both battery plant workers and smelter workers. Excesses were in both "other hypertensive disease" and "chronic nephritis" categories. Although the former included benign hypertension and malignant hypertension, it was dominated by renal disease, which was mentioned in 22 of 30 certificates. The pattern suggested that both vascular changes and interstitial nephritis were involved.

The observed excesses were in populations that had been heavily exposed to lead; all but four of the renal deaths were in men who had started work before 1950. These findings are consistent with numerous studies in animals and in man (6-13).

It was surprising that these cohorts showed no significant excess deaths from either hypertensive heart disease or from vascular lesions of the central nervous system. One would have expected such excesses if low level lead exposures can cause hypertension (13-15).

The low incidence of renal cancers (with SMRs of 41 and 74), in spite of the strong evidence of nonmalignant nephropathy, is encouraging in view of animal studies and isolated human case reports (16,17).

REFERENCES

- Cooper, W. C. Mortality in employees of lead battery plants and lead production plants, 1947-1980 (final report). The International Lead Zinc Research Report Organization, Inc., New York, NY, project LH-157, 1984.
- Cooper, W. C., Wong, O., and Kheifets, L. Mortality among employees of lead battery plants and lead-producing plants,

- 1947-1980. *Scand. J. Work Environ. Health* 11: 331-345 (1985).
3. Marsh, G. M., and Preininger, M. OCMAP: A user-oriented mortality analysis program. *Am. Stat.* 34: 245-246 (1980).
4. World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death, based on the recommendations of the seventh revision conference, 1955. Geneva, 1957.
5. National Center for Health Statistics. Eighth Revision International Classification of Diseases Adapted for Use in the United States. U.S. Government Printing Office, Washington, DC, 1967.
6. Goyer, R. A., and Rhyne, B. C. Pathological effects of lead. *Int. Rev. Exp. Pathol.* 12: 1-77 (1973).
7. Emmerson, B. T. Chronic lead nephropathy. *Kidney Int.* 4: 1-5 (1973).
8. Lane, R. E. The care of the lead worker. *Br. J. Ind. Med.* 6: 125-143 (1949).
9. Legge, T. M., and Goadby, K. W. *Lead Poisoning and Lead Absorption*. Edward Arnold, London, 1912.
10. Lilis, R., Fischbein, A., Valciukas, J. A., Blumberg, W., and Selikoff, I. J. Kidney function and lead: Relationships in several occupational groups with different levels of exposure. *Am. J. Med.* 1: 405-412 (1980).
11. Morgan, J. M., Hartley, M. W., and Miller, R. E. Nephropathy in chronic lead poisoning. *Arch. Intern. Med.* 118: 17-29 (1966).
12. Selevan, S. G., Landrigan, P. J., Stern, F. B., and Jones, J. H. Mortality of lead smelter workers. *Am. J. Epidemiol.* 122: 673-683 (1985).
13. Wedeen, R. P., Maesaka, J. K., Weiner, B., Kipat, G. A., Lyons, M. M., Vitale, L. F., and Joselow, M. M. Occupational lead nephropathy. *Am. J. Med.* 5: 630-641 (1975).
14. Batuman, V., Landy, E., Maesaka, J. K., and Wedeen, R. P. Contribution of lead to hypertension with renal impairment. *N. Engl. J. Med.* 309: 17-21 (1983).
15. Pirkle, J. G., Schwartz, J., Landis, J. R., and Harlan, W. R. The relationship between blood lead levels and blood pressure and its cardiovascular risk implications. *Am. J. Epidemiol.* 121: 246-258 (1985).
16. Baker, E. L., Jr., Goyer, R. A., Fowler, B. A., Khettry, U., Bernard, D. B., Adler, S., White, R. D., Babayan, R., and Feldman, R. G. Occupational lead exposure, nephropathy and renal cancer. *Am. J. Ind. Med.* 1: 139-148 (1980).
17. Lilis, R. Long-term occupational lead exposure, chronic nephropathy, and renal cancer: A case report. *Am. J. Ind. Med.* 2: 293-297 (1981).