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Epidemiological Aspects of Occupational Lead Poisoning

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Introduction

Lead is an ancient metal [1], and the toxic effects of heavy exposure to lead have been recognized in the Western world for more than 20 centuries [2-4]. In recent years a major concern in occupational medicine has been to define the toxicity of lead at lower levels of exposure. Investigations conducted since 1970 have demonstrated that lead causes hematologic, neurologic, and renal impairment in lead workers at exposure levels that previously were considered to be safe [5-7].

In this report we describe three recent epidemiological studies of occupational lead exposure. Our purpose in each instance was to evaluate dose-response relationships between blood lead levels and lead toxicity, particularly at lower levels of occupational lead exposure.

The plants

Two of the studies were conducted in secondary lead smelters. The first of these smelters was located in Memphis, Tennessee and employed 84 workers. In the 11 months preceding our investigation it had recovered 11,500 tons of lead, most of it from used automobile storage batteries. The second smelter, in Salt Lake City, Utah was much smaller and employed only 20 workers. In the 6 months before our evaluation, it had smelted 258 tons of lead. Both smelters had high labor turnover, and median duration of employment at each was less than one year.

The third facility studied, a lead pigment plant in Joplin, Missouri employed 74 workers. It produced lead oxides (red lead and litharge), lead silicate, lead sulphate, and lead peroxide. The workforce at this plant was much more stable and had a median employment of 20 years.

Evaluation methodology

We conducted brief environmental evaluations at the Tennessee and Utah smelters and obtained personal (breathing zone) air samples on selected workers. At the Utah plant, we also collected area air samples.

We performed medical evaluations at each plant, and we interviewed and examined 77 (92%) workers at the Tennessee smelter, all 20 (100%) at the Utah smelter, and 53 (72%) at the Missouri pigment plant. Also, we evaluated one recently discharged employee in Tennessee and nine recently discharged workers. We did not know workers' blood lead levels or exposure histories at the time of medical evaluation.

Medical interviews sought the following items: complete occupational history; a history of symptoms in the preceding year; and a history of past episodes of lead poisoning or of chelation therapy. Medical examination focused on the nervous system, and any abnormal findings were required to be confirmed by a second physician; only those findings judged abnormal by both examiners were recorded.

A venous blood sample was obtained from each worker for lead, hemoglobin, hematocrit, and erythrocyte protoporphyrin (EP) analyses. To evaluate kidney function, serum samples were obtained for determination of blood urea nitrogen (BUN). Blood lead analyses were performed by atomic absorption spectrophotometry. EP levels were determined by fluorescence analysis[8].

Results

Environmental Data

At the Tennessee plant, air samples on 16 production workers showed a range of breathing-zone air lead exposures from 120 ug/M^3 to 350 ug/M^3. At the Utah plant, the mean air lead level in the plant office was 60 ug/M^3, in the lunchroom 90 ug/M^3, and in the furnace room 100 ug/M^3 with the furnace shut down and 2650 ug/M^3 during charging of the furnace.

Blood Lead Data

Blood lead levels at the three plants ranged from 16-280 ug/dl. Fifty-two (67%) of the 78 workers evaluated in Tennessee, 44 (83%) of the 53 tested in Missouri, and 23 (79%) of the 29 studied in Utah had lead levels $\geq$60 ug/dl. Highest levels were found in maintenance and production workers, lowest in office and laboratory personnel.

Clinical Data

Clinical manifestations of lead poisoning were evident at all three plants. In the smelters, with their poorly controlled air lead exposures and rapid labor turnover, symptoms tended to be relatively acute, and symptom prevalence increased with duration of employment. The dominant findings were colic, gastrointestinal symptoms, anorexia, fatigue, myalgia, joint pain, and extensor muscle weakness (Table 1). Symptoms were particularly severe at the Utah plant, and two workers there had possible lead encephalopathy. At the Missouri pigment plant, symptoms were more chronic and the dominant findings were fatigue, joint pains, and myalgia. The most striking finding at this plant was a high prevalence of elevated blood urea nitrogen (BUN).

Dose-response relationships between blood lead levels and clinical findings

At both smelting plants positive associations were evident between the prevalence rates of clinical findings and blood lead levels. Workers who reported symptoms consistent with lead poisoning had significantly higher blood lead levels than workers without such symptoms. At the Tennessee plant no workers with blood lead levels below 40 ug/dl had extensor muscle weakness or gastrointestinal symptoms. By contrast, 5 (13%) of 38 workers with blood lead levels of 40-79 ug/dl, and 14 (54%) of 26 with levels $\geq$80 ug/dl had such findings (Figure 1). At the Utah plant, symptoms were reported by three (38%) of eight workers with blood lead levels below 80 ug/dl, by seven (78%) of nine with levels of 80-99 ug/dl, and by all 12 (100%) with levels $\geq$100 ug/dl.

In the Missouri pigment plant no correlation was found between symptom prevalence rates and blood lead levels. Potential confounding factors were, however, the long duration of workers' exposure to lead and the use of oral chelation therapy.

Relation of blood lead levels to hematological abnormalities

EP concentrations were found to correlate positively (r = 0.76) with workers' blood lead levels. Increases in EP concentrations above background values were first seen at blood lead levels of 40-60 ug/dl.

Anemia, defined as a hemoglobin concentration of $<$14.0 gm/dl, was seen in 27 (21%) of 129 workers studied. A positive dose-response relationship was evident between blood lead levels and the prevalence of anemia (Figure 2). No cases of anemia were found among workers with blood lead levels below 40 ug/dl. One case was found in workers with lead levels of 40-59 ug/dl; six cases were found in workers with levels of 60-79 ug/dl; and 20 cases were found in workers with blood lead levels of 80 ug/dl and above.

Relation of blood lead levels to renal function abnormalities

Elevated BUN levels ($\geq$20 mg/dl) were found in six workers in Tennessee, in five in Utah, and in 17 in Missouri. Elevated BUN values ranged from 21-44 mg/dl. All azotemic workers, except for three in Utah, had been exposed to lead for at least four years. Blood lead levels at the time of evaluation were not significantly higher in azotemic than in non-azotemic workers.

Detailed renal function evaluations were undertaken of the 17 azotemic workers at the Missouri plant as well as of two additional men there with borderline elevations of BUN (Table 2). Nine of these 19 men were found to have previously received oral chelation therapy; six had received multiple courses, and one had been chelated 13 times. Six of the workers were found to be hypertensive (blood pressure above 140/90 mmHg) either by history or during examination. Eight had diminished creatinine clearance ($<$91 ml/min/1.73 m^2 body surface area). Eight had diminished renal concentrating ability (inability to concentrate urine to $\geq$800 mosmol/litre after overnight water fast). Urinary B_2-microglobin levels were strikingly elevated in two workers (993 and 4890 ug/litre). Urinary amino acid screening by thin-layer chromatography was within normal limits in all 19 men.

Discussion

In this study we examined dose-response relationships between blood lead levels and lead toxicity. We were particularly interested in determining whether or not toxicity occurred in workers with blood lead levels below 80 ug/dl and thus within the range of values previously considered safe.

We found evidence of clinical and biochemical lead toxicity in workers with blood lead levels between 40 and 80 ug/dl. Toxicity was most clearly evident in the workers at the two smelters. In those workers, gastrointestinal symptoms and extensor muscle weakness first became evident at blood lead levels between 40 and 59 ug/dl and increased further in frequency at levels above 60 ug/dl. Elevations in EP and cases of anemia also became evident at blood lead levels above 40 ug/dl and rose progressively in frequency and severity with further increases in the blood lead level.

Dose-response relationships were much less clearly evident among workers at the Missouri pigment plant who had a mean lead exposure of 20 years. This lack of association may reflect the presence in those workers of large skeletal lead stores; in such workers, blood lead levels probably are influenced more by release of stored lead than by current exposure [10,11]. The extensive use of oral chelating agents in these workers may also have altered dose-response relationships.

The data from this study support proposals to lower the permissible biological limit for the blood lead concentration to 40 ug/dl [12]. Our data are also consistent with the findings of other investigators who have noted clinical [13,14], hematological [15], and neurological [6,15] impairments in lead workers at blood lead levels below 80 ug/dl.

A particularly disturbing finding in recent investigations of occupational lead toxicity, although not sought in this study, has been the detection of subtle, but apparently irreversible dysfunction of the central nervous system (CNS) at blood lead levels as low as 40 to 60 ug/dl. Several investigators have noted dose-response relationships between occupational lead exposure and psychological dysfunction[16,17]; particularly affected were tests of visual intelligence and of visual-motor activity. Also noted have been slowed reaction times [18] as well as impaired memory, attention, and concentration. These findings have led to speculation that some cases of presenile dementia may be caused by chronic exposure to lead [19].

Our finding of renal dysfunction in 28 workers with occupational exposure to lead, nine of whom gave a past history of oral chelation therapy, parallels previous reports [20-22]. All of those previous studies suggest that relatively prolonged, high-dose exposure to lead is required to produce lead nephropathy; it has also been suggested that repeated use of oral chelation therapy may enhance the severity of the renal effects of lead. The natural history of lead nephropathy is poorly understood. However, a recent analysis of mortality in a cohort of 7032 lead smelter and battery workers in the United States [23] found evidence of excess mortality from chronic nephritis in both groups (standardized mortality ratios of 264 and 175, respectively). These data suggest that lead nephropathy may be an underrecognized problem among long-term lead workers.

In summary, we found evidence in this study for clinical, hematological, neurological and renal impairment in lead workers many of whom had blood lead levels between 40 and 80 gu/dl. Such findings suggest that blood lead levels in lead workers should not exceed 40 ug/dl, a value already more than two standard deviations above the mean for adult males in the United States [24].

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Table 1. Frequency of abnormal clinical findings in lead workers at 3 plants - United States, 1975, 1976.

Findings	Tennessee Smelter(78)*	Utah Smelter(29)*	Missouri Pigment Plant(53)*
Fatigue	19 (24%)	8 (28%)	19 (36%)
Colic	13 (17%)	19 (66%)	1 (2%)
Gastrointestinal symptoms**	17 (22%)	18 (62%)	3 (6%)
Anorexia	18 (23%)	12 (41%)	--
Myalgia	15 (29%)	7 (24%)	6 (11%)
Joint pain	22 (28%)	4 (14%)	10 (19%)
Objective tremor	2 (3%)	4 (14%)	2 (4%)
Extensor muscle weakness	10 (13%)	0	2 (4%)
Possible encephalopathy	0	2 (7%)	0
Anemia	12 (15%)	11 (38%)	4 (8%)
BUN elevation	6 (8%)	5 (17%)	17 (32%)

*Number of workers studied.
**Includes nausea, vomiting, diarrhea, and constipation.

Table 2. Results of renal function tests, Missouri lead plant, 1976

Subject	Age (yr)	Duration of lead exposure (yr)	Blood lead level (ug/dl)	BUN* (mg/dl)	Hypertension	Creatinine clearance (ml/min/ 1.73 m^2)	Fasting urine osmolality (mosmol/litre)	No. of courses of oral EDTA**
1	56	7	154	44	+	85		8
2	48	20	66	30	+	142		0
3	37	20	35	29	+	82	871	1
4	47	23	71	29	+	72	588	4
5	45	8	87	25		128	1020	2
6	53	23	61	24	+	91	1025	9
7	52	26	61	25	+	115	650	0
8	38	20	123	22		109	608	0
9	60	25	75	26		75	278	0
10	42	21	66	25		96	1180	0
11	47	7	48	23		108	820	0
12	53	29	96	20		89	708	0
13	35	13	56	21		109	965	0
14	62	16	105	20		97	912	1
15	52	25	78	23		73	286	1
16	53	20	92	22		108	912	13
17	51	7	80	21		65	704	4
18	52	31	55	19		43	652	
19	29	4.5	58	18		112	1114	

*Arithmetic mean of duplicate determinations in March and May, 1976.
**EDTA, Ethylene diamine tetraacetic acid chelation therapy.

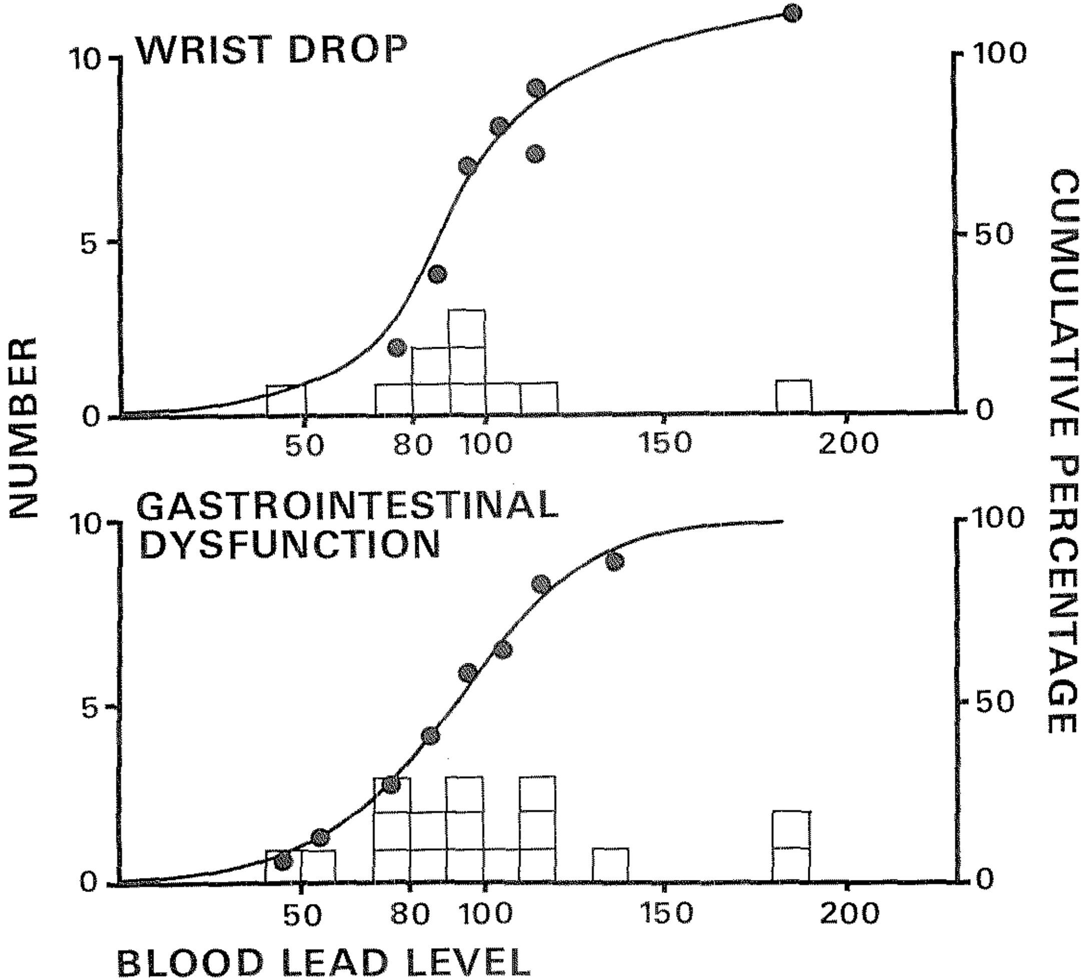

Fig. 1 Number and cumulative percentage of workers with symptoms and signs, by blood lead level, Memphis, Tennessee, 1975.

FIGURE 2

PREVALENCE OF DEPRESSED HEMOGLOBIN VALUES BY BLOOD LEAD LEVEL IN ADULT WORKERS - UNITED STATES, 1975 - 76