Reduction of Blood Lead Levels in Battery Workers by Zinc and Vitamin C

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A group of 39 storage battery workers was evaluated in terms of pertinent biochemical parameters with regard to duration and degree of occupational exposure to lead. Twenty-two of the group had recognized toxic blood lead levels of greater than 60 mcg/100 ml, but fully 31 exceeded the Center for Disease Control's upper limit of normal for erythrocyte protoporphyrin. Other abnormal values found were decreased hemoglobin, increased serum and whole blood copper, increased serum uric acid, decreased serum inorganic phosphate and increased blood spermine, a new lead-related parameter not reported on previously. The severity of lead poisoning among these workers as revealed by blood lead and several other parameters was not related to the duration of exposure (number of years employed), but only to the degree of exposure (job location within the plant).

The battery workers were placed on a regimen of vitamin C and zinc. Twenty-two of the group were followed while on this regimen for a period of 24 weeks. The mean blood lead level for the group dropped from an initial level of 67.6 ± *14.9 mcg/100 ml to 46.0 ± 14.9 mcg/100 ml after 24 weeks. There was also a significant increase in the mean hemoglobin level and a significant decrease in the mean serum and whole blood copper levels with treatment. These changes were striking in view of the fact that they were achieved while the workers were on the job and constantly exposed to high levels of lead.*

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In a recent study we examined the blood lead levels of some 1,000 psychiatric outpatients (Sohler et al., 1977). Their mean lead level was 15.6 mcg/100 ml (range 3.8 -53 mcg/100 ml). The small percentage of patients (5.9 percent) who had lead levels above 25 mcg/100 ml were treated with zinc and vitamin C for several weeks, and in nearly every instance there was a significant decrease in blood lead levels. Since blood lead levels seemed to respond to such a regimen in subjects not occupationally exposed to lead, we investigated the effects of zinc and vitamin C on lead workers who have lead-induced biochemical changes.

Concern has been voiced recently that employers in some lead-using industries have been using chelating agents such as EDTA and penicillamine to reduce lead levels in lieu of efforts to reduce lead levels in the air (Finklea, 1976; Lilis and Fischbein, 1976). Although chelation therapy may have a place in treatment of acute lead poisoning, routine oral prophylactic use can cause problems equal to those imposed by lead itself. The use of a vitamin C and zinc regimen in lead workers may be a desirable alternative to such prophylactic measures in cases where environmental exposure is unavoidable.

The present report is concerned with the effect of these nutrients on a group of battery workers who, depending on job location, have varying degrees of lead exposure.

METHODS

Subjects of the study were 39 volunteers from a battery plant. The purpose and protocol of the study were explained to them, and informed consent was obtained. The subjects ranged in age between 28 and 60 years, and they had been employed by the plant for periods ranging between four and 34 years with a mean duration of 17 years.

At each visit heparinized blood, serum, and urine were collected. On whole blood, lead was determined by the method of Hessel, 1968; erythrocyte protoporphyrin (EPP) by the procedure of Hanna et al., 1976; polyamines by the method of lliev et al., 1967; and the Beutler et al. (1963) procedure for glutathione. Blood copper was determined on a trichloroacetic acid extract by atomic absorption spectroscopy.

Atomic absorption spectroscopy was used to determine serum zinc, copper, and iron according to the method of Olson and Hamlin, 1969.

Aliquots of serum were also sent to Diagnostic Sciences, Inc., Morristown, N.J., for a SMAC 22 diagnostic profile. This included the following determinations: inorganic phosphate, glucose, blood urea nitrogen, uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, lactic dehydrogenase, serum glutamic oxaloacetic transaminase, creatinine, serum glutamic pyruvic transaminase, triglycerides, sodium, potassium, chloride, and CO_2. Zinc and copper in urine were determined by atomic absorption spectrophotometry on undiluted urine samples, and lead in urine was determined according to the method described by Perkin-Elmer, 1971.

The battery workers were put on a daily regimen of 2 g vitamin C and 60 mg zinc (from zinc gluconate). It was recommended that they take half the dose A.M. and half P.M. with meals. Of the original 39 workers, 22 completed the study by staying on the regimen and returning for retesting after 6, 12, and 24 weeks.

When necessary, values of biochemical parameters were compared to values obtained on a control group consisting of 100 males who had no record of lead exposure.

RESULTS

Lead Status and Other Biochemical Parameters of 39 Storage Battery Workers

Blood lead levels for the 39 storage battery workers on their first visit to our center ranged between 36 and 89 mcg/100 ml, and the mean level was 62.1 ± 13.8 mcg/100 ml. Table 1 shows mean levels of blood lead and other affected parameters compared with controls. There was no correlation between age or length of exposure and blood lead or any other hemotological or biochemical parameter.

Although only 22 of these men had over 60 mcg/100 ml lead in blood (the new Labor Department maximum standard for lead in blood, just reduced from 80 mcg/100 ml), 31 had erythrocyte protoporphyrin levels > 60 mcg/100 ml RBC (considered to be the upper limit of normal at the Center for Disease Control) indicating toxicity of lead on heme metabolism in red blood cells. The mean erythrocyte protoporphyrin level was 140.6 ± 112.5 mcg/100 ml, ranging between 17 and 516 mcg/100 ml RBC. The erythrocyte protoporphyrin levels were found to in-

TABLE 1

Mean blood lead and other biochemical parameters in 39 battery workers

Assay	Lead workers	Controls In = 100)
Blood lead mcg/100 ml	62.1 ± 13.8	15.6 ±5.5
Hemoglobin g/100ml	13.4 ±0.87	15.3 ±1.2
Erythrocyte protoporphyrin mcg/100 ml RBC	140.6 ± 112.5	< 20
Serum uric acid mg/100 ml	6.4 ±1.3	5.6 ±1.4
Serum inorganic phosphate mg/100ml	2.6 ±0.33	2.9 ±0.71
Whole blood spermine mcg/ml	1.77 ±0.56	1.56 ±0.44
Serum copper mcg/100 ml	112.6 ±16.7	107.0 ±23.7
Whole blood copper mcg/100 ml	102.4 ± 18.2	90.7 ± 16.3

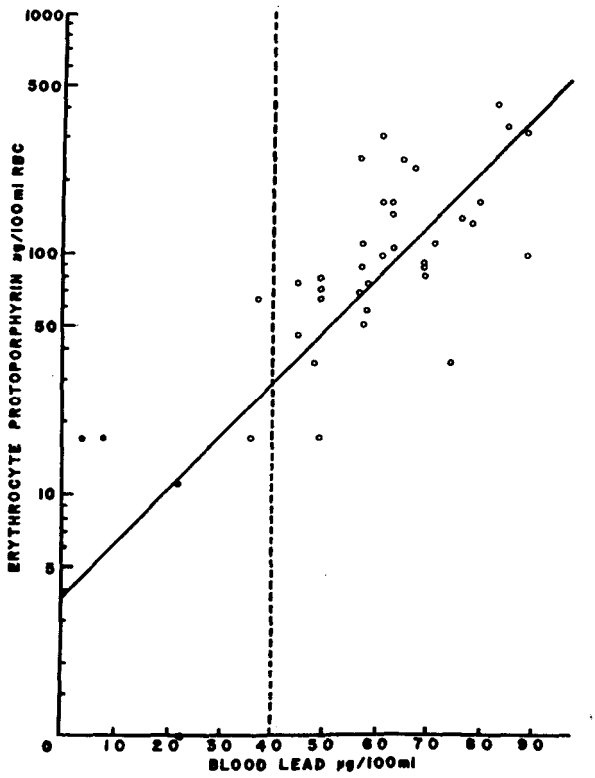
crease logarithmically with increases in blood lead ($r = 0.53$, $p < 0.001$, Figure 1 and Table 2). The mean hemoglobin level for the workers was 13.4 ± 0.87 g/100 ml vs. 15.3 ± 1.2 for the 100 male controls. There was no correlation between hemoglobin and blood lead.

Lead has a strong affinity for sulfhydryl groups; hence it seemed worthwhile to examine such metabolites as might be vulnerable to sulfhydryl group interference. We, therefore, investigated blood levels of spermine and spermidine for whose synthesis S-adenosyl methionine is a precursor, as well as levels of reduced glutathione, found to be decreased in workers exposed to manganese (Jonderko et al., 1971). We also looked at blood histamine levels, both because it has been reported that histidine, from which it is derived via decarboxylation, is elevated in lead workers (Gerber and Gerber, 1977), and because sulfhydryl groups are involved in the conversion to its major catabolite, methyl histamine. Spermidine, histamine, and reduced glutathione levels did not differ significantly from the control group. The mean spermine level of the lead workers was 1.77 ± 0.56 mcg/ml and appeared elevated by comparison with our control group which had a mean of 1.56 ± 0.44.

Serum zinc and iron levels did not differ from the control group, but serum copper levels were very slightly elevated (Table 1). The mean whole blood copper level was higher for the lead workers, 102.4 ± 18.2 mcg/100 ml, vs. 90.7 ± 16.3 for the controls.

Of all the parameters included in the SMAC profile, only the serum uric acid and serum inorganic phosphate levels appeared different for the lead workers. Their mean serum uric acid was 6.4 ±1.3 mg/100 ml vs. 5.6 ±1.4 mg/100 ml for the controls. Their mean serum inorganic phosphate seemed slightly depressed, 2.6 ± 0.33 mg/100 ml vs. 2.9 ± 0.71 mg/100 ml for the controls; out of the 39 men, 15 had levels < 2.5 mg/100 ml. (Diagnostic Sciences reports a normal range of 2.5 - 4.5 mg/100 ml).

FIGURE 1



Correlation between erythrocyte protoporphyrin concentration and blood lead levels ($n = 40$; $r = .53$; $p < 0.001$). Closed circles represent control subjects not exposed to lead. Open circles are battery workers.

TABLE 2 Relationship between blood lead levels and other parameters

Table 2 shows the mathematical correlation between blood lead levels and these parameters. In order to better evaluate whether differences in mean levels of biochemical parameters between lead workers and controls are lead related, the workers were divided into four categories of exposure by job location as follows:

AREA	EXPOSURE	JOB LOCATION
4	Very high	Pasting and mixing
3	High	Assembly
2	Medium	Casting
1	Low	Finishing

Table 3 presents data on the effect of job location on biochemical parameters. As expected, there is a progressive decline in mean blood lead levels with decreasing exposure. There is also a dramatic progressive decline in erythrocyte protoporphyrin with exposure. Hemoglobin and inorganic phosphate levels are consistently low and seem to be unrelated to job location. Uric acid levels decline progressively from a high of 6.8 to 5.4, similar to the control level. Thus, although the correlation between uric acid and blood lead levels ($r = 0.28$) was not statistically significant ($p<0.1$), the categorization according to lead exposure allows one to conclude with some confidence that the changes in uric acid levels are lead related. Spermine levels are elevated in areas 4, 3, 2 and drop to the control levels in low lead Area 1. There seems to be no clear relationship between serum copper and job location, but whole blood copper levels are high in areas 4 and 3 and drop to control levels in areas 2 and 1.

TABLE 3

Blood lead and other biochemical parameters in 39 battery workers categorized by job location

		Area 4 Pasting and Mixing	Area 3 Assembly	Area 2 Casting	Area 1 Finishing	Controls
Number of subjects		**20**	**6**	**8**	**5**	**100**
Assay						
Blood lead	Mean	70	59	58	43	16
(mcg/100 ml)	SD	± 10.6	± 15.2	± 10.9	± 6.3	± 5.5
Hemoglobin	Mean	13.6	12.2	13.1	13.7	15.3
(g/100 ml)	SD	± 0.70	± 0.66	± 0.80	± 0.55	± 1.2
Erythrocyte protoporphyrin	Mean	167	159	101	49	20
(mcg/100 ml RBC)	SD	± 129.0	± 115.1	± 69.9	± 29.1	
Serum uric acid	Mean	6.8	6.5	6.0	5.4	5.6
(mg/100 ml)	SD	± 1.32	± 1.04	± 0.93	± 1.29	± 1.40
Serum inorganic phosphate	Mean	2.6	2.7	2.7	2.6	2.9
(mg/100 ml)	SD	± 0.35	± 0.26	± 0.34	± 0.22	± 0.71
Whole blood spermine	Mean	1.76	2.05	1.92	1.53	1.56
(mcg/ml)	SD	± 0.62	± 0.63	± 0.49	± 0.27	± 0.44
Serum copper	Mean	116	112	102	112	107.0
(mcg/100 ml)	SD	± 16.7	± 15.6	± 15.0	± 18.5	± 23.7
Whole blood copper	Mean	107	107	93	94	91
(mcg/100 ml)	SD	± 20.8	± 14.5	± 8.4	± 18.3	± 16.3

Effect of Vitamin C and Zinc on 22 Storage Battery Workers

Table 4 lists the 22 lead workers who maintained the vitamin C and zinc regimen, their ages, number of years employed in the lead industry, their job locations, and blood lead levels during the 24-week course of treatment. The men were at their posts within the designated work areas for the entire duration of the 24-week study (and for one year prior) except for a two-week period, the 18th to 20th week, when the plant was closed for vacation. Examination of company records showed that blood lead levels for the participants did not fluctuate significantly or unidirectionally over a one-year period prior to commencement of the zinc and vitamin C regimen, nor was there any apparent change following the previous summer's two-week shutdown.

Upon completion of the study 19 out of 22 workers experienced a decline in blood lead; one dropped fully 35 mcg/100 ml, six dropped more than 20 mcg/100 ml, and nine more than 10 mcg/100 ml. Two men showed no change, and only one had a small increase. Those men with the highest initial lead level experienced the greatest change; there was a significant correlation between the extent of decrease in blood lead and the initial blood lead level ($r = 0.65$, $p < 0.005$, Table 2). The histograms in Figure 2 show the distribution of lead levels at 0, 6, 12, and 24 weeks. We see that 12 subjects had blood lead levels over 60 mcg/100 ml on the initial visit. After 24 weeks on the zinc and vitamin C regimen only four men still had in excess of 60 mcg/100 ml lead. In fact this drop to four men occurred within the first six weeks of

TABLE 4

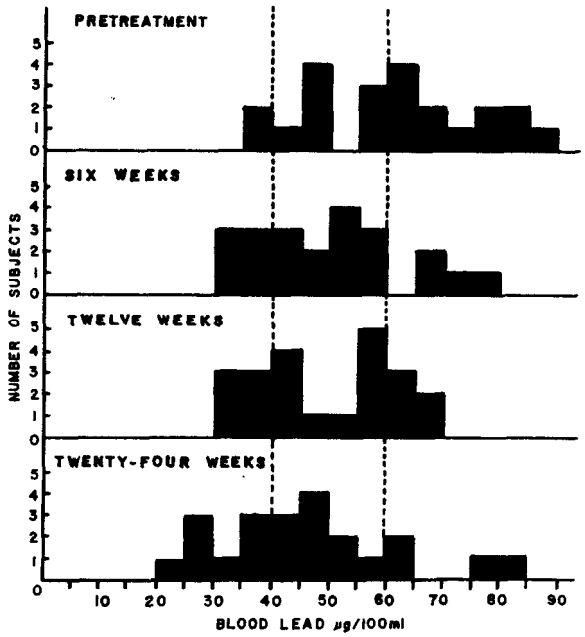
Blood lead in 22 lead workers during treatment with zinc and vitamin C

Subject [1] No.	Age	Exposure to lead (years)	Job Location [2]	Lead (mcg/100 ml) Weeks			
				0	6	12	24
1	42	14	4	89	66	60	82
2	54	8	3	85	75	60	50
3	50	26	4	83	79	64	61
4	51	29	2	78	70	64	54
5	33	10	4	76	55	68	62
6	41	4	4	71	57	64	76
7	50	14	4	69	53	56	43
8	54	15	4	69	51	52	50
9	36	16	4	63	55	48	45
10	48	28	3	63	44	36	39
11	46	9	4	61	57	60	54
12	40	10	4	61	48	44	46
13	31	10	2	58	48	56	39
14	37	9	4	58	44	39	46
15	38	15	3	57	59	68	57
16	51	34	1	49	40	32	29
17	49	32	1	49	40	44	39
18	59	9	4	49	40	44	29
19	28	6	2	49	35	32	32
20	50	29	1	45	44	44	45
21	59	31	1	37	33	32	24
22	48	28	1	36	35	36	29

[1] In order of decreasing zero time lead levels

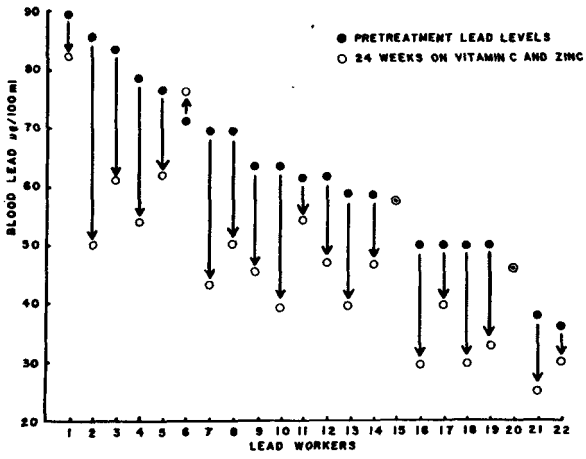
[2] See p. 98 of text.

FIGURE 2



Distribution of blood lead levels in battery workers during treatment with zinc and vitamin C.

FIGURE 3



Change in blood lead levels of 22 battery workers after 24 weeks on a regimen of zinc and vitamin C.

treatment. Whereas there were only two men with under 40 mcg/100 ml lead on the initial visit, this figure increased to six men after 6 and 12 weeks and to eight at 24 weeks. Figure 3 is a pictorial representation of the change in blood lead of each of the 22 lead workers after 24 weeks on zinc and vitamin C.

Table 5 shows mean levels of blood lead and other relevant parameters of the study group within 0, 6,12, and 24 weeks of taking zinc and vitamin C and compares them with control levels. The paired t-test was used to evaluate changes during the course of treatment, and those found to be significant are indicated. A significant drop ($p < 0.001$) in mean blood lead from 61.6 mcg/100 ml to 51.4 occurred within the first six weeks of treatment. Both serum and whole blood copper levels decreased. Serum iron remained virtually unchanged during the 24 weeks of treatment. Serum zinc levels increased in the first six weeks of therapy from 112.6 to 143.0 mcg/100 ml, demonstrating the initial rise we normally see in subjects beginning zinc supplementation, and then fell back characteristically to normal levels by 24 weeks. There was no correlation between the extent of rise in zinc and fall in lead.

Mean hemoglobin levels increased somewhat to 14.8 and 14.3 g/100 ml by 12 and 24 weeks respectively ($p<0.01$). None of the remaining parameters which distinguished the lead workers from the controls, such as erythrocyte protoporphyrin, serum uric acid, serum inorganic phosphate, and whole blood spermine, seemed to be affected by the zinc and vitamin C regimen when levels for the entire 22-man study group were considered (Table 5). Table 6 shows the change in mean levels of blood lead, hemoglobin, erythrocyte protoporphyrin, uric acid, and serum copper at 0, 6, 12, and 24 weeks and in whole blood copper at 0 and 24 weeks as categorized by job location. When the data are examined in this way there seems to be some indication that erythrocyte protoporphyrin is decreasing for the group least exposed to lead. All five men who worked in Area 1 and whose initial EPP levels were 17, 17, 64, 70, and 75, dropped to 0 after 24 weeks. Also, greater drops in serum and whole blood copper occurred with decreasing exposure to lead. Uric acid levels did not respond to treatment for any category of exposure. Since there was no relationship between initial spermine or inorganic phosphate levels and job

TABLE 5

Change in mean levels of blood lead and other biochemical parameters of 22 lead workers on zinc and vitamin C

	Lead workers				Control group n = 100
	Weeks on zinc and vitamin C				
Assay	0	6	12	24	
Blood lead (mcg/100 ml)	61.6 ± 14.9[1]	51.4 ± 12.9*	50.1 ± 12.4*	46.0 ± 14.9*	15.6 ± 5.53
Hemoglobin (gm/100 ml)	13.4 ± .78	----	14.8 ± .98***	14.3 ± 1.6***	15.3 ± 1.2
Erythrocyte protoporphyrin (mcg/100 ml RBC)	149.8 ± 132.4	----	149.2 ± 130.3	146.4 ± 207.6	< 20
Serum uric acid mg/100 ml)	6.4 ± 1.4	6.3 ± 1.6	6.5 ± 1.5	6.6 ± 1.6	5.6 ± 1.4
Serum inorganic phosphate (mg/100 ml)	2.6 ± 0.33	2.6 ± 0.39	2.7 ± 0.30	2.8 ± 0.46	2.9 ± .71
Whole blood spermine (mcg/ml)	1.81 ± .66	1.83 ± .73	----	1.75 ± .56	1.56 ± .44
Serum iron (mcg/100 ml)	98.3 ± 32.1	97.3 ± 24.7	101.6 ± 31.6	97.5 ± 23.6	100.0 ± 31.0
Serum zinc (mcg/100 ml)	112.6 ± 13.2	143.0 ± 39**	120.4 ± 26.4	113.1 ± 17.8	111.9 ± 24.0
Serum copper (mcg/100 ml)	114.3 ± 13.7	110.3 ± 14.6	105.7 ± 16.6	103.4 ± 19.1**	107.0 ± 23.7
Whole blood copper (mcg/100 ml)	97.7 ± 17.3	----	----	89.0 ± 12.1****	92.1 ± 12.4

P <0.001*; p.<0.005**; p <0.01***; p <0.05****.

(Levels of significance from paired t-test comparing parameters at 6, 12, and 24 weeks with zero time).

[1] ± standard deviation.

category, they were not included in this table.

Table 7 shows mean levels of urinary lead, zinc, and copper during the course of zinc and vitamin C supplementation. There was no essential change in excretion of either lead or copper revealed by the single random urine samples we were able to collect. Zinc excretion did increase significantly (paired t-test) within the first six weeks and was maintained at higher levels throughout the study, an indication that the participants were taking the supplements.

TABLE 6

Change in mean blood lead and other parameters of 22 battery workers on zinc and vitamin C categorized by job location

Assay	Number of Subjects / Weeks on Zinc and Vitamin C	Area 4 Pasting and Mixing	Area 3 Assembly	Area 2 Casting	Area 1 Finishing	Control Group
		11	3	3	5	100
Blood lead	0	68	68	62	43	15.6
(mcg/100 ml)	6	55	59	51	38	
	12	55	55	51	38	
	24	54	49	42	33	
Hemoglobin	0	13.6	12.2	13.1	13.7	15.3
(gm/100 ml)	12	15.1	13.9	14.6	14.9	
	24	13.7	14.4	15.4	14.9	
Erythrocyte protoporphyrin	0	198	203	90	49	< 20
(mcg/100 ml RBC)	12	188	200	135	42	
	24	225	165	83	0	
Uric acid	0	6.8	6.7	6.1	5.4	5.6
(mg/100 ml)	6	6.7	6.1	6.1	5.1	
	12	6.9	6.5	6.5	5.5	
	24	7.0	7.3	6.1	5.5	
Serum copper	0	116	113	115	112	107.0
(mcg/100 ml)	6	112	109	113	101	
	12	110	106	104	96	
	24	109	107	108	85	
Whole blood copper	0	99	103	97	94	92
(mcg/100 ml)	24	97	91	83	79	

TABLE 7

Mean levels of lead, zinc, and copper in urine of 22 lead workers on zinc and vitamin C

ASSAY mcg/100 ml urine	Weeks on zinc and vitamin C: 0	6	12	24
Lead	5.5 ± 4.0	5.8 ± 2.7	6.3 ± 3.2	4.9 ± 2.1
Zinc	53.5 ± 35.5	90.4 ± 58.3**	96.5 ± 61.1**	106.0 ± 58.7*
Copper	4.9 ± 1.5	4.7 ± 1.7	4.2 ± 1.3	6.0 ± 2.6

P <0.001*; p <0.005**

(Levels of significance from paired t-test comparing parameters at 6, 12, and 24 weeks with zero time.)

DISCUSSION

The present investigation, designed to evaluate the effects of a dietary supplement of zinc and vitamin C on a group of lead workers, yielded striking results considering that the men were being treated and observed during the course of their continued exposure. The most pronounced effect of the 24-week zinc and vitamin C regimen was the significant reduction of blood lead levels.

Blood lead concentrations are commonly accepted as the best or only practical indicator of "internal dose" (Committee on Toxicology, 1976) although they are not necessarily the best indicator of toxicity. Such indicators for lead which reflect derangement of hemoglobin synthesis in the erythroid cells of the bone marrow, and are reversible, are: increased urinary 6 -aminolevulinic acid, increased urinary coproporphyrin, increased erythrocyte protoporphyrin, decreased ALAD activity and anemia. Of these, we investigated only hemoglobin and erythrocyte protoporphyrin levels. Hemoglobin levels were lower than normal controls and showed a significant increase with zinc and vitamin C supplementation. Although we found, in accordance with other investigators, a strong correlation between pretreatment erythrocyte protoporphyrin and lead levels, there was seemingly no improvement, i.e., decrease of erythrocyte protoporphyrin with decreased lead levels during the course of treatment except that shown by Area 1 workers. It would be most interesting to repeat the study over a much longer time period, monitoring as many of the reversible physiological correlates of lead intoxication in blood and urine as possible; 24 weeks may be too short a time to note changes in such reversible lead effects.

Another probable effect of lead, not reported on previously, are the elevated whole blood spermine levels we found in all categories of lead exposure except low-lead Area 1. The exact biological function of the polyamines is unknown, but increased synthesis occurs in a number of systems characterized by rapid tissue growth, and increased concentrations of these compounds in physiological fluids is thought to reflect rapid cell turnover (Raina et al., 1976). Considering the decreased survival time of the red blood cell due to lead (greater fragility of RBC membrane) and the inhibitory effects of lead in heme synthesis, anemia is not so severe as would be expected, and it is thought that there is a compensatory increased hemoglobin synthesis and production of erythrocytes (Goyer and Rhyne, 1973a). During erythropoiesis there is an increased rate of nucleic acid synthesis, and spermine levels increase during rapid nucleic acid synthesis. Thus, if erythropoiesis is more rapid in lead-intoxicated individuals, this might be reflected in higher than normal spermine levels.

Other indicators which we found to be related to lead in our study group were increased serum uric acid levels and decreased serum inorganic phosphate; neither were altered with treatment. Hyper-phosphaturia in acute lead posioning and hypophosphatemia in children (Goyer and Rhyne, 1973b) have been reported and are related to dysfunction of proximal renal tubules; elevated blood uric acid levels and gout have long been associated with chronic renal disease among lead industry workers. These parameters are probably irreversible because they reflect permanent renal system damage.

Since heavy metals exert some of their effects in biological systems by substituting for essential trace metals, the trace metals zinc and iron in serum, and copper in serum and whole blood were measured initially in the 39 lead workers to see whether they differed from controls as a result of lead exposure, and also to assess whether zinc therapy would affect trace metal levels as well as the toxic lead levels. Only copper levels are affected both by lead exposure and by the treatment. It was to be expected that whole blood copper levels would be more meaningfully related to lead exposure than serum copper since 90 percent of the blood lead is associated with the erythrocytes; indeed, other workers have found an increase in erythrocyte copper in lead poisoning (Rubino et al., 1958). Perhaps determination of copper in washed

erythrocytes would be a more sensitive indicator of lead effects as well as of prevention and recovery. That the treatment lowered copper levels either according to the well-known zinc-copper antagonism or because of vitamin Cs effect on decreasing absorption of dietary copper (Spivey Fox, 1975) is an added bonus in view of the recent definitive study that high dietary copper exaggerates lead toxicity (Cerklewski and Forbes, 1977). It is worth mentioning here that the general population may be suffering from borderline zinc deficiency and excess copper (Mertz, 1972; Sandstead, 1973; Scheinberg, 1961). Such dietary metal imbalances, if common, would have more profound consequences for the lead worker. We may consider whether the lead toxicity of disproportionate severity occurring in alcoholics may not be due to their penchant for a high-carbohydrate hence low-in-zinc diet.

Urinary data showed no increase in excretion of lead with the treatment which did effectively lower blood lead levels. Although certainly no firm conclusions can be drawn on the basis of one random urine sample taken every six weeks, these data are consistent with a.hypothesis that the zinc and/or vitamin C are preventing the absorption of lead from the gastrointestinal (G.I.) tract.

A definitive study published while our investigation was in progress reported that as dietary zinc increased, the severity of lead toxicity in the rat decreased (Cerklewski and Forbes, 1976). The evidence included decreased lead concentration in the blood, liver, kidneys, and tibias, and favorable changes in all the adversely affected hematological parameters. Injected zinc had no effect whatever, injection of zinc prior to lead dosing did not alter lead toxicity, and urinary lead excretion was not affected by zinc. The study concluded that the protective effect of zinc was inhibition of lead absorption at the intestinal level. In a subsequent paper these authors postulate that the exaggeration of lead toxicity by supplemental dietary copper may be a secondary effect. Since both zinc and copper bind to a metallothionein-like protein in the rat duodenum and compete for absorption, they feel copper may be preventing zinc from exerting its protective effect (Cerklewski and Forbes, 1977). There is other evidence, however, from in vivo and in vitro animal studies that high dietary zinc might afford protection against lead already absorbed. The enzyme 6 -aminolevulinic acid dehydratase (ALAD), involved in an early stage of heme synthesis, is dependent upon dietary zinc for its very synthesis (Finelli et al., 1974). It is itself a zinc metalloenzyme which is inactivated with exposure to lead, and its activity can be restored both in vivo and in vitro by zinc (Abdulla and Haeger-Aronsen, 1974; Finelli et al., 1975). Thus, disturbed heme synthesis could be restored by zinc.

Our use of vitamin C was prompted by human and animal studies which have been reviewed by Sohler et al., 1977. Although the mechanism and site of its interaction with heavy metals remain to be elucidated, it appears that heavy metals do cause an increased utilization of ascorbic acid (Chatter-jee et al., 1975). Therefore, requirements of lead workers for vitamin C may be greater and, conversely, low dietary levels of vitamin C might increase a person's susceptibility to toxic effects of lead. Indeed, an early study on the use of vitamin C in lead workers was suggested by the bad conditions of gums common to both scurvy and lead poisoning (Holmes et al., 1939a).

A number of studies (Holmes et al., 1939a; Holmes et al., 1939b; Marchmont-Robinson, 1941) done over 30 years ago reported vitamin C causing observable improvement in clinical and laboratory parameters of workers exposed to particulate lead. A later investigation (Evans et al., 1943) failed to confirm these results, but this study was done on workers exposed to tetraethyl lead. The absorption and metabolism of inorganic and organic lead compounds have been shown to be different (Goyer and Rhyne, 1973c). Therefore, the reduction in blood lead achieved in this study on storage battery workers may not be attainable for those exposed to organic lead.

The pattern of decrease in blood lead

levels, the urinary data, and the work of other investigators suggest that the drop in blood lead levels may be due to interference in the absorption of newly ingested lead. Most of the drop in blood lead levels occurred within the first six weeks of treatment and was sustained at essentially the same levels over the next 18 weeks. It may be instructive to review a study in which workers with only recent exposure (two to four weeks) had mean Jead levels of about 53 mcg/100 ml, those with long exposure and subclinical intoxication, 64 mcg/100 ml, those with clinical intoxication, 78 mcg/100 ml, and those with previous clinical intoxication who had no exposure to lead for at least 18 months, 56 mcg/100 ml (Secchi and Alessio, 1974). Another study reports that lead levels of workers newly entering employment climb to about 60 mcg/100 ml within three weeks and level off for the duration of the 12-week study (Benson et al., 1976). Their mean and range is similar to our group who were exposed to lead between four and 34 years. It appears that there is a rapid ascent in blood lead to saturation, or to the level of stable lead binding sites in the blood. Above that level lead may be either excreted or deposited in other tissues, an equilibrium being established between blood and tissues. Newly entering lead may occupy some labile fraction of the blood and be the cause of transitory increases and decreases. Thus, those workers who were away from lead for over 18 months and whose lead levels had dropped only to the level achieved by new workers within a few weeks, may have lost only that labile fraction as yet undeposited in tissue. If the prime effect of our proposed treatment is in preventing absorption of new lead, then the levels to which they have stabilized during treatment with zinc and vitamin C may reflect the equilibrium between old body-burden lead and blood. Those workers with the highest lead levels and in the high exposure areas experienced the greatest drop, consistent with this view.

Even if minimizing absorption of new lead is the prime or only effect of the proposed dietary supplements, it will have profound consequences. It is reported that only a minor fraction of airborne inhaled lead particles are retained in the respiratory tract; the remainder are cleared by ciliary action of respiratory epithelial cells and swallowed. Furthermore even retention by the pulmonary compartment may not be equivalent to absorption since a portion of retained particles are cleared by pulmonary macrophages (Goyer and Rhyne, 1973d). Thus effecting interference with absorption at the intestinal level would afford protection against virtually all exposure to particulate lead.

It is likely on theoretical grounds that zinc and vitamin C may also have therapeutic effects, i.e., may protect against lead already absorbed, or mobilize body burden lead and cause it to be excreted. Whether the proposed regimen is therapeutic or prophylactic or both remains to be determined; however, the striking reduction of blood lead levels achieved by these battery workers makes its adoption a judicious option for those with undue lead exposure. * * *

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