Bull. Environ. Contam. Toxicol. (1987) 38:975–980

Bulletin of Environmental Contamination and Toxicology

Lead, Ferritin, Zinc, and Hypertension

C. J. Lockett and D. Arbuckle

Department of Experimental and Clinical Pharmacology, University of Natal, Durban 4001, South Africa

Lead is known to have had deleterious effects on human health for centuries; evidence has been presented that chronic lead poisoning affected the populations of ancient Rome and Egypt. Recently it has been postulated that the absorption of lead and cadmium in amounts too small to produce acute clinical symptoms might nevertheless induce abnormal tissue changes which could eventually lead to hypertension and other cardiovascular disease (Kopp et al. 1980; Schroeder 1967).

The genesis of human hypertension appears to involve the interplay of a variety of causative factors including emotional, psychosomatic, nervous, endocrine and renal changes. The interplay of these factors is extremely complex and is a frequent source of interest to research workers. The possibility that metallic ions are involved in these complex interrelationships through their ubiquitous role as cofactors in important enzyme reactions is suggested by the finding that some chelating agents may reduce raised blood pressure (Schroeder 1967).

Lead is a known neurotoxin and the conduction of nerve impulses may become impaired in peripheral nerves of industrial workers exposed to lead for prolonged periods (Waldron 1980). Behavioural changes and hyperactivity can occur in children and animals exposed to lead even when obvious signs or symptoms of acute poisoning are absent (Rose 1983; Waldron 1980; Silbergeld and Chisholm 1976). The element affects catecholamine metabolism and the renin angiotensin system, and induces hypertension in animals at levels below those associated with its acute toxic effects (Goldman et al. 1981;

*Send reprint requests to C.J. Lockett at the above address.

Bertel et al. 1978; Silbergeld and Chisholm 1976). An apparent association between hypertension and exposure to lead has been reported in man and animals by a number of workers (Victery et al. 1982; Barltrop 1979; Jhaveri et al. 1979; Sharret 1979; Beattie et al. 1976; Beevers et al. 1976).

In view of these relationships, a survey of Black lead workers was set up in a factory near to the University of Natal Medical School.

MATERIALS AND METHODS

Blood pressure and blood lead levels of 120 Black workers in a lead factory were monitored for a period of six months. The blood pressure was measured in the supine position once a month, and the mean blood pressure calculated.

Forty of these workers were chosen at random, and their serum ferritin, calcium, copper, zinc and lead levels were measured. Samples were taken from normal Black and White controls (38 in each group).

The ferritin levels were analysed by radioimmunoassay (Amersham Ferritin RIA Kit method). The calcium, copper, zinc and lead were measured by atomic absorption spectrophotometry. Serum sodium and creatinine were done by Auto Analyser (Beckman Astra method).

Statistical analysis of the results was carried out using an unpaired Student's t-test. Linear regression correlations were plotted for lead, ferritin and mean BP. Incidence of hypertension amongst factory workers was compared, using the Chi-squared test. The limit of significance in all tests was set at $P < 0.05$ on a two-tailed test. Ferritin results were also compared by Wilcoxon analysis.

RESULTS AND DISCUSSION.

The results are shown in Table 1 and Figure 1.

Figure 1 shows that there is no correlation between mean blood pressure and blood lead. Table 1 shows that ferritin levels were higher in Black control workers than in White controls, $P < 0.05$. There was no significant correlation between blood lead and ferritin levels. There was a significant correlation between ferritin and mean blood pressure levels of the Black lead workers, $P < 0.05$. In the group of Black lead workers with high blood pressures, significantly higher

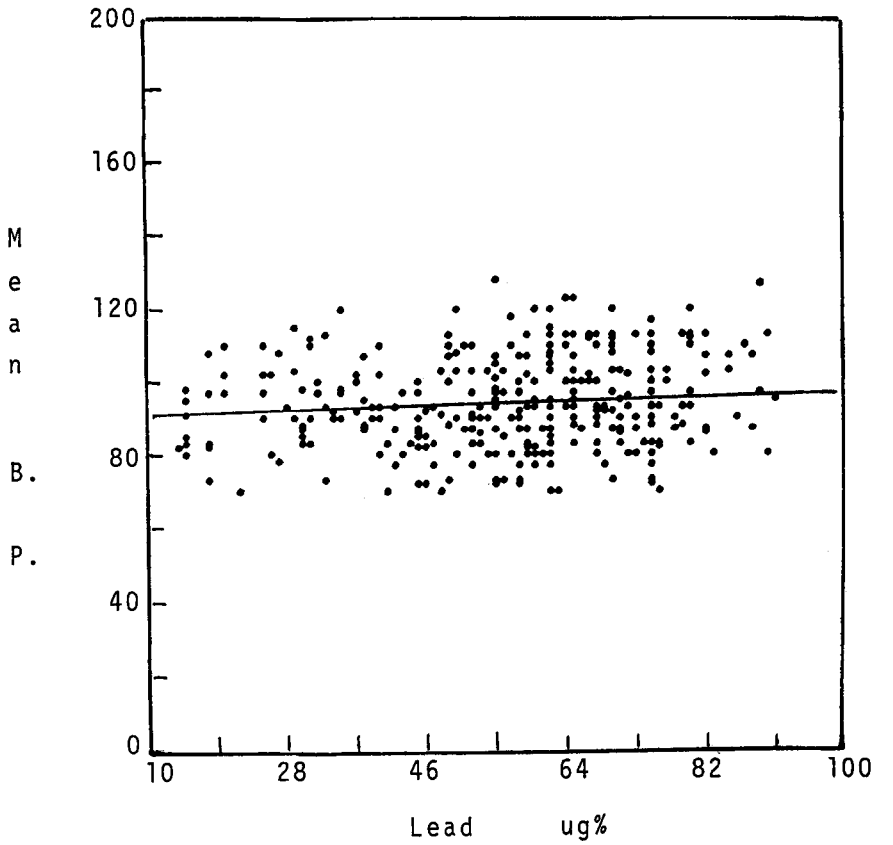

Figure 1. Serum Lead vs. Mean B.P.

ferritin levels were found, $P < 0,02$. Zinc levels of Black lead workers were significantly higher than White controls, $P < 0.001$.

The possibility that lead effects are influenced by iron metabolism and may therefore be related to the iron balance of the individual was examined. The African Black is known to have high iron levels, and our results confirm this. Iron inhibits intestinal absorption of lead, and iron deficiency would be expected to enhance lead intoxication (Jacobs and Worwood 1980; Munro and Linder 1978; Six and Goyer 1972). Our findings suggest that an abundance of iron may have the opposite effect and inhibit the lead toxicity leading to higher blood pressure.

Essentially all enzymes in the haem biosynthetic pathway are inhibited by lead, probably through the binding of metal to SH groups.

Table 1. Serum levels of Black Lead Workers and Black Controls and White Controls (Mean ± Standard Deviation).

SERUM LEVELS	BLACK LEAD WORKERS		BLACK CONTROLS		WHITE CONTROLS	
FERRITIN ug/l	196	(171)	413	(455)*	152	(119)*
CALCIUM mmol/l	2.41	(0.095)	2.54	(0.12)	2.49	(0.17)
CREATININE umol/l	86	(14.7)	96.2	(22.5)	108	(21.26)
SODIUM mmol/l	142	(5.5)	140.3	(1.8)	146.5	(2.24)
POTASSIUM mmol/l	4.7	(0.44)	4.1	(0.34)	4.15	(0.31)
CHLORIDE mmol/l	107	(2.5)	108.8	(2.8)	108.3	(3.65)
B.P. DIASTOLIC	82	(14)	84.3	(9.6)	75	(9.4)
B.P. SYSTOLIC	118	(15.4)	121.9	(13.3)	118	(10.9)
BLOOD LEAD ug%	61.8	(16.2)*	19.8	(5.4)*	29.45	(12.19)*
UREA mmol/l	4.9	(1.4)	3.6	(1.7)	4.5	(0.63)
COPPER ug/ml	1.22	(0.36)	1.21	(0.11)	1.03	(0.11)
ZINC ug/ml	1.39	(0.27)*	0.98	(0.16)*	1.0	(0.11)*
MAGNESIUM ug/ml	21.0	(2.7)	19.9	(1.6)	20.4	(0.70)
WEIGHT Kg	73.1	(13.3)	68.8	(12.2)	76.0	(6.4)
AGE	38	(10.6)	36.0	(9.2)	22.0	(2.0)

* FERRITIN (WHITE CONTROLS/BLACK CONTROLS) : $P < 0.05$ (WILCOXON)

* LEAD (WHITE CONTROLS/BLACK LEAD WORKERS) : $P < 0.001$
* ZINC (WHITE CONTROLS/BLACK LEAD WORKERS) : $P < 0.001$ (UNPAIRED T STATISTIC)

Iron also inhibits erythrocyte uptake of lead, and lead competes for intracellular iron-binding sites, so that it may limit intracellular accumulation of iron. Lead-induced anaemia and the associated reduction of serum iron concentration may be prevented in rats by the administration of copper, but copper deficiency seems to promote the anaemia which results from the lead administration. Copper also stimulates ferrochelatase activity and reverses the inhibition of solubilized mitochondrial preparations of this enzyme produced by lead. The precise effects of lead on the final step of haem biosynthesis may not principally involve the enzyme ferrochelatase itself, but rather cytochrome oxidase, either directly or through effects on copper, thus preventing reduction of iron to the ferrous form.

The serum zinc levels of the Black lead workers were significantly higher than those of the White controls, P <0,001. This could be due to genetic factors, again possibly affording protection from the hypertensive effect of lead.

Although our results did not show significant differences between the magnesium levels of controls and Black lead workers, it has been shown that magnesium supplementation in rats decreases retention and increases excretion of lead (Silbergeld and Chisholm 1976).

The issue of whether a lifetime of continuous exposure to these chemical pollutants, either alone or in combination with factors such as nutrition, can accelerate degenerative cellular tissue changes, so leading to hypertension and cardiovascular disease, is still controversial.

REFERENCES.

Barltrop D (1979) Geochemical and man-made sources of lead and human health. Phil Trans R Soc Lond B288:205-211

Beattie AD, Campbell BC, Goldberg A, Moore MR (1976) Blood lead and hypertension. Lancet 2(7975):1-3

Beevers DG, Erskine E, Robertson M, Beattie A, Campbell BC, Goldberg A, Moore MR, Hawthorne VM (1976) Blood-lead and hypertension. The Lancet, 3 July 1976:1-3

Bertel O, Buhler FR, Ott J (1978) Lead-induced hypertension: blunted beta-adenoceptor-mediated functions. Brit Med J, 4 March 1978; 551.

Goldman J, Vander A, Mouw D, Keiser J, Nicholls MG (1981) Multiple short-term effects of lead on the renin-angiotensin system. J Lab Clin Med 97:251-263

Jacobs A, Worwood, M (eds) (1980) Iron in biochemistry and medicine, II. Academic Press, New York

Jhaveri RC, Lavorgna L, Dube S, Glass L, Khan F, Evans H (1979) Relationship of blood pressure to blood lead concentrations in small children. Pediatrics 63(4):674-676

Kopp SJ, Perry HM, Glonek T, Erlanger M, Perry E, Barany M, Dargros AL (1980) Cardiac physiologic-metabolic changes after chronic low level heavy metal feeding. Amer J Physiol 239(1):H22-30

Munro HN, Linder MC (1978) Ferritin structure, biosynthesis and function. Physiological Reviews 58(2):317-527

Rose J (1983) Trace elements in health: A review of current issues. Butterworths, London

Schroeder HA (1967) Cadmium, chromium and cardiovascular disease. Circulation 35:570-581.

Sharret AR (1979) The role of chemical constituents of drinking water in cardiovascular diseases. Amer J Epidemiology 110(4):401-418
Silbergeld E, Chisholm J (1976) Lead poisoning: altered urinary catecholamine metabolites as indicators of intoxication in mice and children. Science 192:153-155
Six KM, Goyer RA (1972) The influence of iron deficiency on tissue content and toxicity of ingested lead in the rat. J Lab Clin Med 79:128-136
Victery W, Vander A, Shulak J, Schoeps P, Julius S (1982) Lead hypertension and the renin-angiotensin system in rats. J Lab Clin Med 99(3):354-362
Waldron H (1980) Metals in the environment. Academic Press, New York

Received October 20, 1986; accepted January 15, 1987.