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Evaluation of the effect of lead exposure on the liver in Egyptian lead tank welders

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With 2 tables

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Chronic kidney disease and arteriosclerosis in lead workers of many years standing was believed by the early observers to be a direct though delayed consequence of their occupational exposure (4). In experimental lead poisoning *Ying Han Hsu* (46) suggested that lead poisoning would cause hypertension before arteriosclerosis. Arteriosclerosis was most apparent in heart and brain, then spleen and adrenal glands. However, a group of 50 workers who were occupationally exposed to lead for 5 years showed no clinical abnormalities or serum lipid values which would indicate the premature development of atherosclerosis (32). Certain reports have been published also on the effect of lead on the liver, however, the opinions of authors vary greatly, while some of them cast doubt on the hepatotoxicity of lead in industrially exposed workers (30, 40).

Others reported their investigations showing a toxic effect of lead upon the liver (6). These differences in opinions stimulated us to study the changes in serum lipids and some of the liver function tests which may elucidate the effect of lead on the liver in a group of Egyptian lead tank welders who were exposed to lead fumes for periods up to 22 years.

Materials and methods

The material of the present study is composed of a group of 16 lead tank welders who were admitted to our Institute for periodical medical examination. Their age ranged between 28 and 50 years and they were exposed to lead fumes for periods up to 22 years. They were clinically free from any sign or symptom of lead poisoning and also free from any parasitic infestation. Their medical reports revealed no present or past history of liver disease. A control group of 10 healthy workers who have never been exposed to lead and are of the same social class were similarly investigated.

The following investigations were carried out on both exposed and control groups.

Determination of whole blood lead as an index of lead exposure and absorption, blood haemoglobin level and urinary delta amino levulinic acid (ALA).

Determination of serum glutamic oxaloacetic transaminase (GOT) serum glutamic pyruvic transaminase (GPT), alkaline phosphatase (Alk phosph) and lactic dehydrogenase (LDH), as well as total bilirubin, total protein and albumin fraction.

Serum total lipid, triglycerides, cholesterol, phospholipid and lipoprotein pattern were also determined.

The method of *Keenan* et al. (19) for the determination of lead in blood has been applied in the present work. Urinary ALA determination was carried out according to the method of *Grabecki* et al. (12). The acid haematin method of *Sahli* (35) was used for determination of blood haemoglobin. Concerning the serum enzymes, the method of *Reitman* and *Frankel* (33) was used for determination of serum glutamic pyruvic and glutamic oxalacetic transaminases. Serum alkaline phosphatase was estimated by the method of *King* and *Armstrong* (20). The method of *Wroblewski* (45) was used to determine serum lactic dehydrogenase activity. Total serum proteins were determined by the biuret method and electrophoretic separation of serum proteins was done according to *King* and *Wootton* (21).

Lipids were extracted from plasma according to the method of *Folch* et al. (9). The phase containing lipid was evaporated to dryness. The lipid was redissolved in chloroform and aliquots were used for further analysis. Triglycerides were determined by the method of *Van Handel* and *Zilversmit* (41). An aliquot of the extract was taken for phospholipid analysis. Inorganic phosphate was determined by the method of *Morrison* (31). Total cholesterol in plasma was measured by the method of *Bloor* (3). And total lipid was measured according to the method of *Swahn* (36).

Results and discussion

Lead poisoning is a syndrome caused by the toxic action of lead which may be seen in people whose tissues contain higher than normal amounts of lead. Lead poisoning may occur by ingestion or by inhalation of lead dust or fumes. The metabolism of lead follows closely that of calcium particularly with regard to its deposition in and mobilization from bone (4). A relatively high lead content was also found in the liver of patients suffering from acute manifestations of lead poisoning (39).

Lead in common with other heavy metals has a variety of toxic actions on protoplasma; the most precisely described are on certain enzyme systems and on cell membrane (5).

In rats poisoned with lead acetate ultrastructural changes in liver cells indicated a disequilibration of metabolic processes. Mitochondria and cytoplasm were mainly affected with marked myelinic degeneration of cytoplasm (13).

In the present work the absence of clinical abnormalities in the exposed group shows that the exposure has not reached a dangerous level.

However, the danger of continual absorption of lead in amounts which do not of themselves cause clinical symptoms and signs of poisoning is that a point may be reached when the "threshold level" for potential poisoning can be exceeded and/or intercurrent factors causing lead mobilization from bone may cause a sudden outbreak of clinical symptoms of lead poisoning (4). Estimation of the level at which lead absorption has become potentially dangerous usually depends upon examination of the blood or anaemia, for a raised lead content and the urine for increased excretion of delta amino levulinic acid (ALA). It was shown that the blood lead level is probably the most valuable indication of excessive lead absorption (28).

It is shown in table 1 that the lead level in blood of the present exposed group was significantly increased and the blood haemoglobin level was significantly more decreased than the control values.

Table 1.

Parameter	Pb	Hb	ALA	GOT	GPT	ALK	LDH	Total	Protein g/100 ml		
Group	µg/100 g	%	mg/L	IU/L	IU/L	phosph. KAU	IU/L	Bilirubin mg/100 ml	Total	Albumin	A/G ratio
Control	27.50	95.0	3.85	± 18.7	14.7	6.72	87.60	0.84	7.09	4.24	1.48
10 subjects	± 7.15	± 4.3	± 1.29	± 5.9	± 4.8	± 2.15	± 10.62	± 0.18	± 0.69	± 0.57	± 0.20
Lead Exp.	42.19	87.18	7.60	43.58	51.4	9.54	109.0	0.99	5.07	2.24	0.74
16 subjects	± 9.81	± 3.19	± 3.00	± 16.51	31.4	± 9.64	± 22.9	± 0.24	± 0.64	± 0.40	± 0.15
P	< .05	< .05	< .05	< .05	< .05	> .05	< .05	> .05	< .05	< .05	< .05

Mean ± S. D.

The results also indicated a significant increase of urinary excretion of ALA in lead exposed group.

It is suggested that lead may decrease the haemoglobin level by inhibiting a multienzyme systems involved in haem biosynthesis (17), e.g. the enzyme delta amino levulenic acid dehydratase (ALA-dehydratase) which catalyses the formation of porphobilinogen from two molecules of delta amino levulenic acid (ALA) (17). It was found that one of the most sensitive index of lead exposure is the estimation of the activity of the enzyme delta aminolevulinic acid dehydratase (1). However, several studies have shown that present day level of environmental lead contamination are sufficient to produce inhibition of ALA-dehydratase (16). *Frank* et al. (10) suggested that the increased urinary excretion of delta aminolevulenic acid (ALA) in lead intoxication was the only reliable indicator of the health hazard involved.

The present results revealed also a statistically significant increase of both transaminases GOT and GPT as well as lactic dehydrogenase (LDH) in the exposed group of workers. However, no significant change was observed in both serum alkaline phosphatase and total bilirubin.

Increased serum GPT and GOT were found to be very sensitive indices of hepato-cellular injury (37). Also high levels of serum (LDH) have occasionally been found in hepatocellular disease (44).

The present results for transaminases are in agreement with those reported by many authors (14, 42). Opposite results however have been reported by others (43).

In experimental poisoning with lead, *Kruster* et al. (26) found a transient increase in hepatic lead associated with transient stimulation of serum lactate and glutamate dehydrogenase.

Also, it is clear from table 1 that total proteins are diminished in the lead exposed group, and that the decreased albumin fraction in mainly responsible for the inversed A/G ratio. These findings agree with that of many authors (18, 25).

Although the present results revealed a slight increase is serum alkaline phosphatase and total serum bilirubin of the exposed workers, yet this increase was not statistically significant. These results are not in harmony with those of *Urbanska-Bonenberg* (40), who found a diminished alkaline-phosphatase activity and hyperbilirubinemia in the serum of lead poisoned animals. These controversies most likely reffect differences in the degree of exposure.

The effect of lead exposure on serum lipids are shown in table 2. There is a slight increase in serum total lipid in general, yet a significant increase of serum triglycerides and a significant decrease of phospholipids were found in lead exposed group, while cholesterol showed a tendency to increase. Thus the phospholipid/cholesterol ratio was lowered in thirteen cases out of fifteen cases examined. Concerning the lipoprotein pattern a significant increase was found in B-lipoprotein and thus the B/α ratio increased.

Konikova (23) studied the metabolism of cholesterol and phospholipids in 49 cases exposed to lead. Increase in cholesterol and a decrease of phospholipid levels were found in cases with lead intoxication.

Table 2. Serum Lipids.

		Triglycerides mg/100 ml	Phospholipid mg/100 ml	Total cholesterol mg/100 ml	P/C ratio
Control	m	175	260	163.2	1.60
Group	SD	± 42	± 58	± 20.8	± 0.18
	n	(5)	(5)	(5)	(5)
Exposed	m	250.37	174.54	179.45	0.978
Group	SD	± 62.93	± 51.19	± 35.79	± 0.288
	n	(19)	(14)	(15)	(13)
P		< .05	< .05	> .05	< .05

Lipoprotein pattern

	Total lipids mg/100 ml	α lipoprotein	β lipoprotein	γ lipoprotein	B/α ratio
Control Group	501.1	147.0	291.2	43.2	1.97
n = (16)	± 56.1	± 18.7	± 28.5	± 13.8	± 0.22
Exposed Group	609.2	127.1	433.3	52.87	3.40
n = (16)	± 220.4	± 36.5	± 107.5	± 20.27	± 1.38
P	> .05	> .05	< .05	> .05	< .05

Duff et al. (7, 8) and others (29) suggested that a lowering of the phospholipid/cholesterol (P/C) ratio in the plasma parallels the degree of atherosclerosis present. The main blood lipid changes believed to play a role in production of atherosclerosis are an increased cholesterol, triglycerides (22) and prebeta lipoproteins (15).

Since no clinical abnormalities were recorded in the exposed group of the present work. And it was suggested that lead poisoning would cause hypertention before arteriosclerosis (46).

Thus the increase in serum triglycerides and B-lipoprotein together with the lowering of the phospholipid/cholesterol ratio (table 2) may indicate premature development of atherosclerosis. Fatty liver may result from reduction of lipoprotein formation in the endoplasmic reticulum, which is related to removal of triglyceride from the liver (34). *Fumiyo* et al. (11) showed that triglyceride was secreted as lipoprotein in the early stage of experimental fatty liver. They suggested that ultrastructural changes of the endoplamic reticulum is associated with the abnormal accumulation of fat in the liver.

Also, is experimental poisoning with lead, changes in the smooth endoplasmic reticulum of the hepatocytes and lysosomes were found to occur (26). The studies of *De Duve* (2) have implicated the lysosomes in the development of hepatic necrosis and autolysis. Indirect evidence of liver damage was also provided in the present study by the increase in serum GOT, GPT and LDH enzymes besides the decreased albumin/globulin ratio. It was shown that serum transaminase, lectate dehydrogenase, and

cholinesterase activities showed early increase with increasing liver weight. They serve as indicators of the progress of liver fattening (38).

Thus the present results may indicate the beginning of fatty infiltration of the liver, as well as premature development of atherosclerosis in subclinical lead poisoning. It is concluded therefore that lead poisoning may have a vascular as well as hepato-toxic action.

Summary

In a group of Egyptian lead tank welders who were exposed to lead fumes for periods to 22 years the changes in serum lipids and some of the liver function tests which may elucidate the effect of lead on the liver were investigated.

The results revealed increased blood lead level associated with decreased blood haemoglobin and increased urinary excretion of delta amino levulinic acid. However, no clinical abnormalities were recorded in the exposed group of the present work. Thus the increase in serum triglycerides and B-lipoprotein together with the lowering of the phospholipid/cholesterol ratio which were found may indicate premature development of atherosclerosis. Indirect evidence of the beginning of liver fattening was also provided by the increase in serum GOT, GPT, LDH enzymes and decreased albumin/globulin ratio besides the changes in serum lipid values. It is concluded therefore that lead poisoning may have a vascular as well as hepato-toxic action.

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