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The interaction between lead and essential trace elements in mice through F_1-generation.

By

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ABSTRACT

The present study was designed to investigate the effects of lead on maternal, paternal, and F_1-generation iron, zinc, copper, and manganese levels in the liver, kidney, and brain. Besides, lead residue levels were determined in the same tissues. Male and female mice were exposed to 0.0026, 0.026, and 0.26% lead acetate (14.2, 142, and 1420 ppm lead) via drinking water up to 70 days. In addition, a cross-mating trial was conducted. Analysis showed that the level of hepatic, renal, and brain lead was considerably reduced during pregnancy and lactation periods compared to that in nonpregnant state. Also hepatic, renal, and brain lead was reduced in postmated males compared to premated males. The changes of Cu, Zn, Mn, and Fe concentrations in tissues of premated male and female mice were similar to those induced by lead in postmated male and female mice during gestation and lactation periods. No effects appeared on the concentrations of elements in F_1-female mice for the kidneys and brain compared to the control group and F_1-male mice. Residual lead was shown in the tissues of F_1-female which produced from some combined groups, compared to the control. The levels of lead residual significantly increased in the liver of F_1-male mice in some of combined groups compared to the control.

INTRODUCTION

Pregnancy causes many physiological changes in maternal body, such as hemodilution (Bentley 1985), increase of blood volume (Hytten, 1985), enlargement of liver (Reis *et al*, 1988) and so on. Alterations are also induced at various biochemical levels, for example increases in pregnancy zone protein (pregnancy associated α_2-glycoprotein) (Sand *et al.*, 1985) and ceruloplasmin (Disilvestro, 1986) and decreases in albumin and zinc (Elizage and Ferreira, 1985) in blood plasma. In addition to the alterations mentioned above some studies observed pregnancy associated decreases of renal copper (Cu) and Zinc (Zn) concentrations in rats (Suzuki *et al.*, 1990). Further, decreases in Cu and Zn in kidneys were attributed to Cu and Zn lost from metallthionein (MT), which suggested that Cu and Zn bound to renal MT may be utilized as a source of fetal supply of the 2 metals (Suzuki *et al.*, 1990).

Lead (Pb) is one of the most toxic and pervasive pollutants in the environment and although there has been some lowering of blood lead levels in recent years, the levels continue to be of concern for African persons with low income, and those with low educational attainment. Lead is known to disturb the normal course of pregnancy, possibly by interaction with the normal maternal-fetal metabolism of essential trace metals such as Cu and Zn (Lin-Fu, 1992). In humans, lead is accumulated and stored in bones (half-life of approximately 62 years, and pregnancy as a condition of calcium stress, may induce changes in bone physiology and mineral metabolism that result in mobilization of lead from bone back into maternal circulation directly to the fetus (Watson *et al.*, 1997, Silbergeld 1991).

Cu and Zn must be transferred intensively from the maternal to the fetal body particularly at the late gestation period to meet the fetal requirements, as in the case of other nutrients. Decreases of Cu and Zn concentrations in the maternal body during pregnancy may be caused by transfer of maternal metal to the fetus, especially lead (Suzuki *et al.*, 1990). The present study was intended to examine whether lead can be

mobilized during pregnancy and transferred from dam to fetus and affected the trace metals concentrations such as Zn, Cu, Mn, Fe. In other words we investigated whether lead affect the levels of an important trace metals in exposed male and female mice during premating, mating, gestation, and lactation periods and their offsprings at concentration levels of lead are equal to those which give no-maternal effects to those giving maternal toxicity according to investigations were previously reported.

MATERIALS AND METHODS

Animals:

180 male and 320 female ICR (CD-1) mice (High Institute of Public Health, Alexandria University, Alexandria, Egypt) were used as F0 generation. Mice were examined for external signs of disease or injury. The animal room was maintained at 25 °C ± 2 °C and a relative humidity of 50 ± 5% with a 12 hr light- dark cycle. Mice were acclimated for two weeks prior to treatment. Standard diet was offered and tap water *ad libitum*.

Test material and treatment:

Lead acetate trihydrate was dissolved in deionized water to give drinking water concentrations of 0.0026, 0.026, and 0.26% lead acetate (14.2, 142, and 1420 ppm lead). Acetic acid (0.00125%) was added to help in dissolution. The control group drinking water was 0.00125% acetic acid in deionized water. These solutions were provided as drinking water *ad libitum* beginning at day 45 of age, designated as day 0 of treatment. The male and female mice were assigned randomly to four study. groups. Eighty females and sixty males were assigned to the control group. Eighty females and forty males were assigned to each of the 14.2, 142 and 1420 ppm of lead exposure groups. Lead drinking water concentrations were available *ad libitum* from glass water bottles fitted with stainless-steel spouts. After approximately 24 hrs, control and test concentrations were discarded and the bottles were refilled with

freshly prepared concentrations. The bottles were replaced with clean ones at weekly intervals.

F_0-necropsy and cross mating :

After 70 days of lead treatment, ten males and ten females from each group were randomly selected to undergo a full necropsy. Liver, kidney, and brain, were removed and stored in nitric acid. In different exposed groups, exposed male mice were mated with unexposed female mice, unexposed males were mated with exposed females, exposed males were mated with exposed females, and unexposed males were mated with unexposed females as shown in Fig.(1). In general, two females were paired with one male up to 15 days without any treatment. Vaginal pluges were daily observed, the day the vaginal pluges were observed was designated Day 0 of gestation. Following confirmation of mating, females were removed from the male's cage and housed individually. The F0 males were anesthetized immediately after mating. The organs (liver, kidneys, and brain) were removed and stored in nitric acid.

Pregnant F0 females were allowed to give birth to the F1 pups (without treatment during gestation and lactation periods), and the day of delivery was designated Day 1 of lactation. Any female did not deliver was presumed not pregnant. After the F_1 pups were weaned, the F0 females were anesthetized. The organs (liver, kidneys, and brain) were removed, and stored in nitric acid.

F_1-generation and mating:

At 90 days age, all F_1 offsprings were aneasthezied and the brain, liver, and kidneys were removed and stored in HNO_3 acid till analysis.

Elements Concentration:

To prepare the tissues for metal analysis, acid digestion was performed by the method of kuhnert *et al.*, 1982, and Sorell and Graziano 1990. Ultrex HNO_3 was pipetted into the Teflon vessels such that the tissue: acid

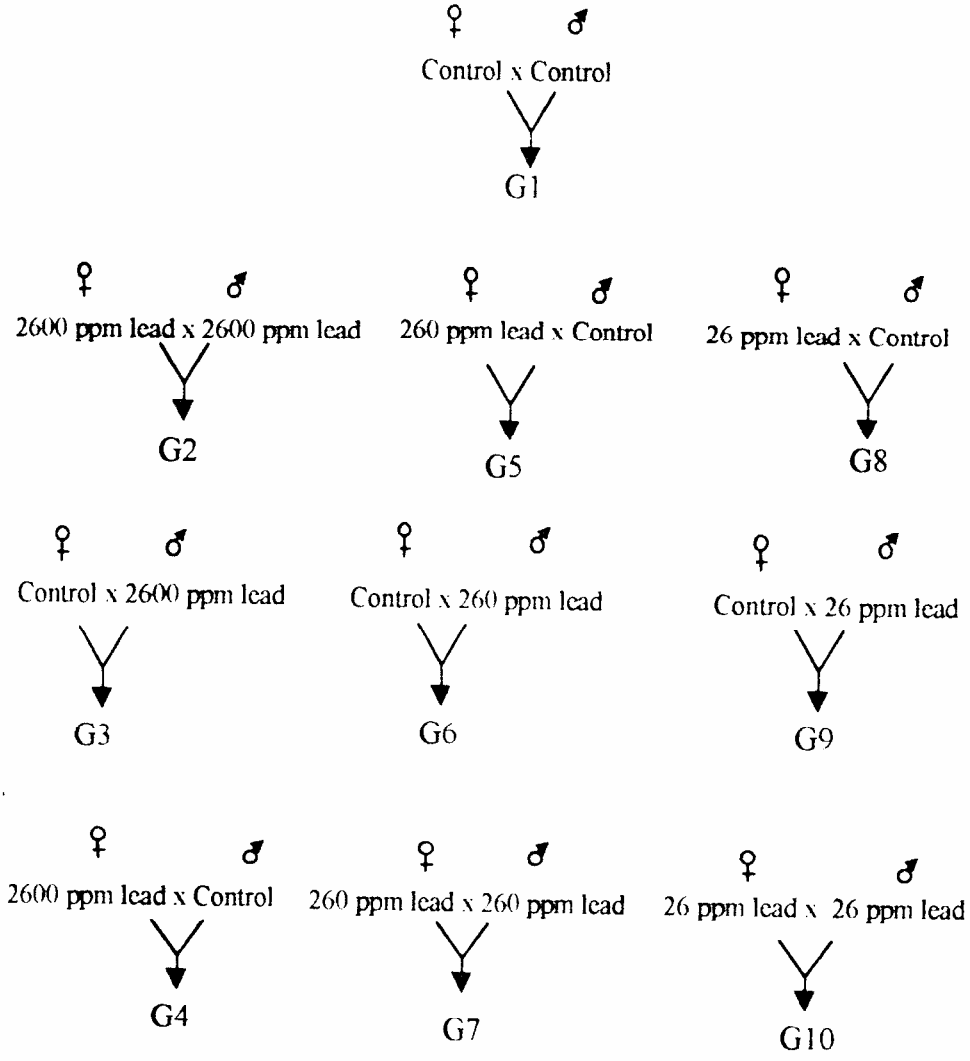

Fig. (1): Scheme of crossmating groups (G_1 , G_2, ... etc.) of control male and female mice (F_o) and exposed male and female mice (F_o) at different concentration levels of lead acetate (ppm) via drinking water.

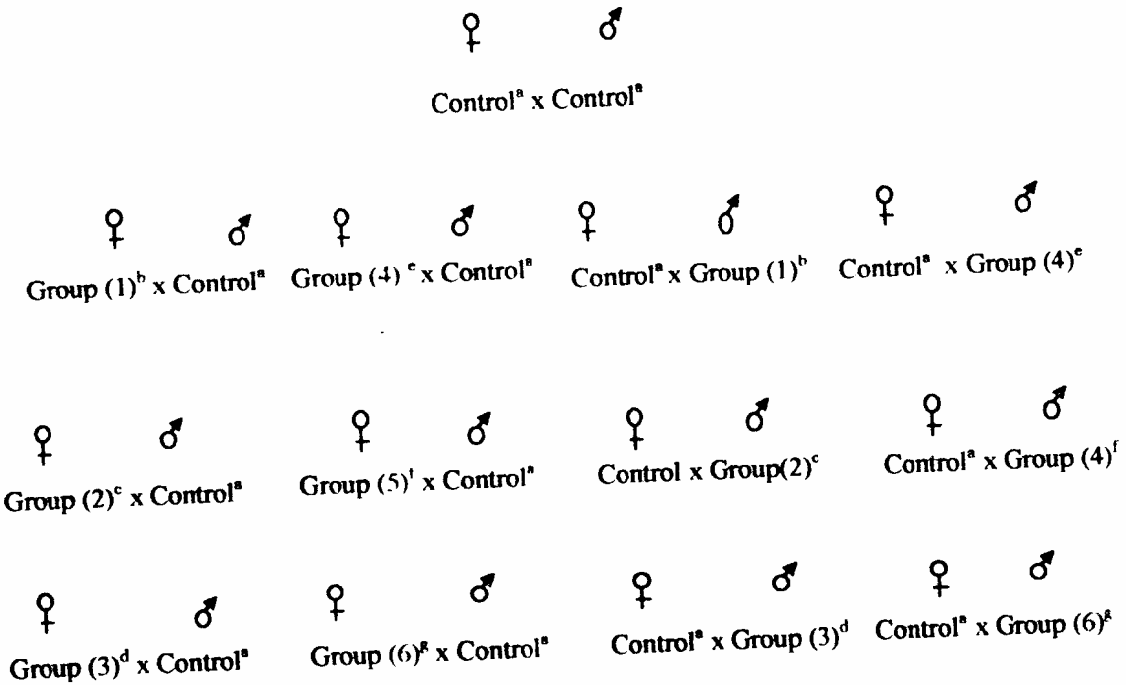

Fig. 2: Scheme of crossmating groups of F_1-male or female mice produced from different F_0-pairing groups. ([a] control female X control male, [b] 2600 ppm lead female X control male, [c] 260 ppm lead female X control male, [d] 260 ppm lead male X control female, [e] 26 ppm lead female X control male, [f] 26 ppm lead male X control female, and [g] 26 ppm lead female X 26 ppm lead male).

ratios 1:3 for complete digestion. The vessels were sealed tightly and placed in an oven at 128°C for approximately 2 hr. After removal and cooling, 0.8 ml of 30% hydrogen peroxide was pipetted into each vessel and, with the lids slightly loose, they were turned to the oven at 128°C and allowed to remain until the samples were completely dry. Once cool, they were reconstituted with the same volume of HNO_3 as in the first step of the digestion and left until all the residue was dissolved. They were then brought up to 10 ml with deionized water. Elements concentrations (Zn, Fe, Mn, Cu, Pb) were determined by atomic absorption spectrphotometry (Perkin-Elmer/3300)(Soil, Water and Environment Research Institute, Alexandria, Egypt).

Statistical analysis.

All statistical comparisons were done using analysis of variance. Intergroup comparisons were made with Scheffe's test for multiple comparisons at an α level of 0.05 (Noursis, 1994).

RESULTS AND DISCUSSION

F_0-Generation in Premating Period.

The changes of elements concentration in premated female and male mice are presented in Tables (1) and (2). Concentrations of iron (Fe) in liver, brain and kidneys were decreased in all the treated groups for both females and males. Zinc concentrations were increased in all the treated groups for liver, in the 0.026, and 0.26% lead acetate treated groups for kidneys and decreased in all the treated groups for brain for both male and female mice. While concentrations of renal and liver copper were increased in the 0.026, and 0.26% treated groups for females, copper concentrations were increased in male liver in all the treated groups. In brain, concentrations of Cu were decreased in all the treated groups for both male and female mice While hepatic manganese (Mn) was decreased only in the 0.26% lead acetate, it was increased in all the treated groups for kidneys and brain for females. In male mice, the concentrations of Mn in liver were increased in all the treated groups.

Table (1).; Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels,and Lead Residues in Different Organs of F_0-Female Mice During Premating Period

Treated Groups[a]	Mean Metal Concentrations-ug/g wet tissue ±SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
0	158.5±35.2	56.3±29.3	5.28±2.2	0.54±0.5	0.35±0.17
0.26	38.13±11.7**	93.98±0.6**	7.02±1.6*	0.19±0.09**	6.75±2.2**
0.026	76.7±20.9**	95.5±12.4**	6.02±1.81*	0.54±0.24	3.60±2.68**
0.0026	106.5±23.8*	89.5±20.7**	5.03±1.86	0.65±0.36	2.36±1.26**
			Kidney		
0	104.40±15.6	6.73±0.8	2.10±0.54	0.47±0.20	0.50±0.37
0.26	45.89±10.5**	14.50±0.41*	4.95±0.37*	0.78±0.26*	8.63±5.15**
0.026	65.05±7.65**	10.13±0.6*	3.57±1.07*	0.71±0.27*	4.14±0.99*
0.0026	83.70±13.6*	7.74±2.22	2.15±0.37	0.76±0.22*	1.10±0.31*
			Brain		
0	63.28±7.28	7.73±2.09	2.24±0.76	0.30±0.05	0.59±0.5
0.26	30.38±4.48**	2.97±1.55**	0.49±0.2**	0.43±0.19*	6.07±1.21**
0.026	35.9±4.90**	2.99±1.04**	0.71±0.14**	0.47±0.18*	4.45±0.97**
0.0026	45.57±6.24*	4.07±0.76**	1.04±0.37*	0.97±0.2**	1.42±0.4*

[a]Lead acetate concentrations (%).

*Significantly different from control value at $P \leq 0.05$.

**Significantly different from control value at $P \leq 0.01$.

Table (2).; Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels, and Lead Residue in Different Organs of F_0-Male Mice During Premating Period

Treated Groups*	Mean Metal Concentrations-ug/g wet tissue ±SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
0	123.6±30.6	43.30±23.3	1.41±0.56	0.54±0.48	0.61±0.48
0.26	30.3±17.0**	52.44±1.63*	4.68±1.93*	0.74±0.12*	7.93±1.95**
0.026	66.1±30.7**	51.16±28.7*	3.00±2.5*	0.70±0.31*	3.60±2.68**
0.0026	76.1±20.8**	47.40±26.7*	2.35±1.31*	0.72±0.57*	2.58±1.91**
			Kidney		
0	122.5±25.7	7.21±2.28	2.21±0.6	1.46±0.89	0.53±0.27
0.26	41.10±3.3**	9.79±1.09*	4.20±0.41*	0.35±0.09*	7.59±3.04**
0.026	53.62±13.1**	8.64±1.2*	3.85±0.14*	0.63±0.31*	2.82±0.73**
0.0026	83.88±1.4**	6.97±1.66	2.27±0.34	1.20±0.73	1.25±0.34**
			Brain		
0	60.30±10.36	6.50±0.74	4.45±0.59	2.62±0.62	0.36±0.25
0.26	38.55±2.76**	2.33±0.61**	0.77±0.3**	0.36±0.21**	6.10±1.4**
0.026	39.80±5.78**	2.66±0.66**	1.11±0.45**	0.84±0.29**	4.70±2.12**
0.0026	39.15±14.71**	3.62±1.38**	1.17±0.49**	1.03±0.47**	1.55±0.67**

*Lead acetate concentrations (%).

*Significantly different from control value at $P \leq 0.05$.

**Significantly different from control value at $P \leq 0.01$.

Since the concentrations of Mn in brain were decreased in all the treated groups, renal Mn concentrations were decreased only in the 0.026, and 0.26% treated groups. Interference of lead with the intestinal iron absorption and the subsequent decreased availability of this essential metal may account for the reduced iron levels in the liver, kidneys and brain in all the treated groups compared to the control (Steibert *et al.*, 1984). The increased concentrations of renal Zinc and Copper in lead treated female mice reported here were believed to indicate a protective role of these metals in the kidneys (Petering *et al.*, 1979). Raised Zn levels in the livers of females resulted from a compensation mechanism which, in response to increasing tissue concentrations of lead which were increased in all organs at all the concentration groups for both female and male mice. This effect might induce apparent disturbances in the copper excretion with bile appear to underlie the elevated copper levels in the livers of lead exposed mice (Ashby *et al.*, 1980). Therefore, copper accumulation may result in liver disease and brain damage leading to clinical neurologic or psychiatric dysfunction (Brewer *et al.*, 1998).

F_0-Females After Gestation and Lactation Periods.

The concentrations of trace elements for F0-females after gestation and lactation periods are presented in Table(3). While iron liver concentrations reduced in all the combination groups of the treated females mated with untreated males, no effects appeared in iron levels in the other combined groups compared to the control. These findings were consistent with the result of Singh *et al.*, 1999 who reported that hepatic Fe levels had a tendency to be lowered during pregnancy when female mice treated with 50 mg/kg/day lead before mating. Hepatic Zinc levels were increased in all the pairing groups of the treated females mated with untreated males compared to the control group and the other pairing groups. Although Zn was mobilized from dams livers during gestation and lactation periods, it was not substantially mobilized from livers of treated dams, which may suggest that Pb inhibited the transfer of Zn to the fetus. Cu concentrations in the livers were increased by Pb treated before mating and conception. However, pregnancy and lactation caused a significant decrease of Cu concentrations in the treated female mice

mated with untreated males. Therefore, the decrease of Cu may be explained by the pregnancy-associated liver enlargement and partly by the decrease of superoxide dismutase with gestation. Mn concentrations in the liver reduced in the pairing groups the control males x the 0.26% lead acetate females, control males x 0.026% lead females, control males x 0.0026% lead acetate females, and the 0.0026% lead acetate males x the 0.0026% lead acetate females compared to the control and the other pairing groups.

Although the hepatic levels of pb were increased in all the combination groups which treated females mated with untreated males compared to the control and the other pairing groups, these levels were lower than those in the liver of treated females before mating. These findings might be attributed to the alteration of the physiological and biochemical status of F_0-females during gestation and lactation periods. Furthermore, the rates and pathway of the metabolic effects of lead might change during gestation and lactation periods. The same trends were observed for all the renal trace elements. Brain levels of Cu and Mn were unaffected in all the pairing groups. The other trace elements levels (Fe and Zn) were in the same trend as liver and kidney levels. Brain Pb concentrations were increased only in the 0.26% ppm lead acetate females x the control males, the 0.026% lead acetate females x the control males, and the 0.0026% lead acetate females x the 0.0026% lead acetate males. Renal pb levels were increased only in the pairing groups of the control males x the 0.26% lead acetate females, and the control males x the 0.026% lead acetate females.

F_0-Males After Mating.

Concentrations of metals are given in Table (4). While lead residue levels increased in all the treated groups for liver and brain and in the 0.026 and 0.0026% lead acetate for kidneys, compared to the control, these levels were lower than those in the male mice before mating. A possible explanation for this finding is that lead was accumulated and stored in bones (half-life of approximately 62 years) (Watson *et al.*,

Table (3)., Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels, and Lead Residue in Different Organs of F_0-Female Mice After Gestation and Lactation Period

Crossmatin Groups	Mean Metal Concentrations-ug/g wet tissue ±SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
1[a]	162.19±14.2	41.90±12	0.73±0.2	0.94±0.44	0.55±0.4
2[b]	24.80±3.3**	55.60±0.6*	0.55±0.2*	0.27±0.1**	4.69±1.4**
3[c]	69.00±19.3**	56.73±2.4*	0.66±0.2*	0.37±0.1**	4.32±1.5**
4[d]	168.46±17.9	41.80±13.3	0.75±2.1	0.90±0.1	0.51±0.2
5[e]	64.80±22.9**	50.41±3.2*	0.53±0.7*	0.75±0.5*	3.36±2.6**
6[f]	163.80±43.3	43.75±23.4	0.77±1.9	0.90±0.2	0.55±0.5
7[g]	72.46±12.7*	55.12±4.4*	0.55±1.4*	0.70±0.2**	1.96±0.7**
			Kidney		
1[a]	102.40±4.7	42.90±7.1	2.65±1.0	0.89±0.1	0.60±0.3
2[b]	55.70±18.3**	58.31±1.4*	0.88±0.1**	0.32±0.2**	1.05±0.4*
3[c]	55.30±6.83**	53.70±5.2*	0.82±0.8**	0.36±0.1**	0.00±0.2*
4[d]	100.75±19.2	42.80±9.9	2.60±0.7	0.85±0.5	0.50±0.19
5[e]	35.90±10.2**	55.34±1.4*	1.28±0.4*	0.45±0.1**	0.68±1.1
6[f]	105.50±8.2	43.10±11.8	2.89±0.1	0.85±0.1	0.60±0.4
7[g]	78.30±5.1*	59.80±12.0*	1.15±0.1*	0.34±0.1**	0.96±0.3

	Brain				
1[a]	70.59±10.5	4.00±0.5	1.60±0.6	0.28±0.1	0.21±0.1
2[b]	50.50±7.2*	5.95±0.1*	1.65±0.1	0.27±0.1	1.00±0.3*
3[c]	57.20±5.1*	5.46±0.2*	1.59±0.3	0.26±0.1	0.64±0.3*
4[d]	73.60±7.14	4.63±0.2	1.60±0.03	0.28±0.1	0.21±0.1
5[e]	51.70±5.9*	5.61±0.3*	1.54±0.4	0.28±0.1	0.21±0.1
6[f]	71.80±4.3	4.09±0.1	1.66±0.04	0.29±0.03	0.22±0.1
7[g]	50.50±4.3*	5.88±0.1*	1.68±0.1	0.24±0.1	0.45±0.1*

Note: lead acetate concentrations (%).

[a]Control female x control male, [b]Control male x 0.26% lead acetate female, [c]Control male x 0.026% lead acetate female, [d]Control female x 0.026% lead acetate male, [e]Control male x 0.0026% lead acetate female, [f]Control female x 0.0026% lead acetate male, and [g]0.0026% lead acetate male x 0.0026% lead acetate female.

*Significantly different from control value at $P \leq 0.05$.

**Significantly different from control value at $P \leq 0.01$.

Table (4) :,Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels, and Lead Residues in Different Organs of F_0-Male Mice After Mating

Treated Groups[a]	Mean Metal Concentrations-ug/g wet tissue ±SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
0	93.4±20.9	37.6±6.8	1.88±0.87	0.63±0.13	0.39±0.25
0.26	47.9±21.4**	38.1±3.2	1.65±0.26	0.65±0.2	4.97±0.91**
0.026	52.4±13.9**	39.4±7.3	1.25±0.41	0.57±0.25	2.14±0.91**
0.0026	86.1±15.5	39.8±4.5	1.43±0.67	0.75±0.3	1.01±0.63**
			Kidney		
0	113.5±17.1	7.91±2.3	2.61±0.61	1.27±0.83	0.56±0.25
0.26	38.42±3.8**	8.48±1.38*	2.92±0.18	1.54±0.29	7.73±1.66**
0.026	47.58±4.6**	7.97±1.6*	2.20±0.38	1.99±0.12	2.06±1.07**
0.0026	84.90±9.4**	7.17±1.38	2.05±0.52	1.45±0.94	0.37±2.42
			Brain		
0	68.28±9.19	6.97±2.36	2.40±1.09	0.64±0.29	0.45±0.1
0.26	35.32±11.91**	5.84±0.68*	0.48±0.22**	0.54±0.07	3.12±1.8**
0.026	63.10±12.33	5.06±1.21*	2.12±0.3	0.51±0.25	2.21±0.89**
0.0026	69.80±10.04	6.38±1.01	2.32±0.87	0.52±0.17	1.01±10.38**

[a]Lead acetate concentrations (%).

*Significantly different from control value at $P \leq 0.05$.

**Significantly different from control value at $P \leq 0.01$.

1997). No effects appeared on the hepatic Zinc, Copper, and manganese levels after mating Hepatic iron levels were decreased in the 0.026, and 0.26% lead acetate compared to the control and 0.0026% groups. Therefore, the trace elements levels (Zn, Cu, and Mn) recovered after mating. The same trend appeared in the levels of renal trace elements. All the elements (Fe, Zn, Cu, Mn) in the brain were decreased in the different treated groups compared to the control. Brain iron and copper levels were decreased only in the 0.26% lead acetate treated groups compared to the control. While brain Zn level was reduced in both 0.26 and 0.026% lead acetate treated groups, the level of Mn in brain was reduced in all the treated groups. The kidneys and brain are major target organs for lead toxicity. Generally, lead induced alteration in the physiological status of the brain (Beck, 1992, Gerhardsson *et al.*, 1998, Gong and Evans, 1997).

F_1-Generation.

Concentrations of metals are given in Tables(5), and (6). Lead residue levels were increased only in F_1-females livers which were produced from the pairing group of control male x the 0.26% lead acetate female, and control male x 0.026% lead acetate compared to the control group. While hepatic iron levels were decreased in the F_1-females which produced from the pairing groups of control male x the 0.26% lead acetate female, and control male x 0.026% lead acetate, Zn, Cu, and Mn levels were increased in the same pairing groups The renal and brain lead levels were increased in F_1-females which produced from the same pairing groups. Renal and brain iron concentrations were decreased only in the F_1-females which were produced from the pairing group of the 0.26% lead acetate x control male. Renal and brain Zn, Cu, and Mn concentrations, were unaffected. Although hepatic lead levels were increased in F_1-males which produced from the pairing groups of the 0.26% lead acetate female x control male, and the 0.026% lead acetate female x control male compared to the control group, all the hepatic trace elements were unaffected in all the F_1-males. No effects on the renal and brain trace elements appeared in all the F_1-males compared to the control A possible explanation for these results is that pregnant mice can be the

Table (5) : Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels, and Lead Residues in Different Organs of F_1-Female Mice.

Gossmating Groups	Mean Metal Concentrations-ug/g wet tissue+ SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
1[a]	140.96±7.1	58.67±4.8	1.03±0.3	1.07±0.3	0.23±0.1
2[b]	95.21±4.8*	99.41±3.9*	2.87±0.05*	1.82±0.1*	2.67±0.6*
3[c]	98.28±3.4*	81.15±1.9*	1.95±0.03*	1.97±0.02*	2.16±0.4**
4[d]	149.24±5.8	60.11±2.6	1.05±0.1	1.69±0.3	0.16±0.1
5[e]	142.18±6.2	61.50±9.8	1.25±0.4	0.95±0.3	0.20±0.1
6[f]	140.30±17.8	63.16±2.1	1.40±0.5	0.95±0.1	0.38±0.1
7[g]	141.10±78	63.92±3.2	1.07±0.3	0.99±0.1	0.31±0.1
			Kidney		
1[a]	89.40±17.0	20.19±2.3	2.12±0.3	1.00±0.2	0.15±0.03
2[b]	75.00±9.1*	20.00±1.0	2.54±0.4	1.00±0.3	0.28±0.1*
3[c]	85.70±9.2	21.00±1.2	2.93±0.4	1.39±0.4	0.22±0.05*
4[d]	85.90±17.8	22.30±3.0	2.24±0.3	1.07±0.2	0.08±0.0
5[e]	86.76±3.6	19.91±1.2	2.10±0.3	1.22±0.5	0.20±0.3
6[f]	87.00±7.1	19.00±1.3	2.99±0.3	1.10±0.2	0.12±0.3
7[g]	88.10±8.6	22.66±2.1	2.96±0.2	1.27±0.4	0.11±0.0
			Brain		
1[a]	52.50±11.18	1.78±0.44	1.00±0.24	0.48±0.09	0.15±0.05
2[b]	32.80±18.5*	1.46±0.26	1.11±0.31	0.57±0.05	1.05±0.37**
3[c]	50.40±6.61	1.36±0.27	1.33±0.35	0.55±0.08	0.97±0.1**
4[d]	57.50±11.6	1.44±0.31	1.07±0.12	0.59±0.13	0.16±0.09
5[e]	51.00±7.86	1.26±0.43	1.02±0.44	0.63±0.18	0.12±0.03
6[f]	50.40±8.46	1.21±0.23	1.31±0.25	0.59±0.13	0.12±0.03
7[g]	49.80±5.39	1.07±0.11	0.52±0.122	1.31±0.29	0.14±0.04

Note: lead acetate concentrations.(%)

[a]Control female x control male, [b]Control male x 0.26% lead acetate female, [c]Control male x 0.026% lead acetate female,
[d]Control female x 0.026% lead acetate male, [e]Control male x 0.0026% lead acetate female,
[f]Control female x 0.0026% lead acetate male, and [g]0.0026% lead acetate male x 0.0026% lead acetate female.

*Significantly different from control value at $P \leq 0.05$.

**Significantly different from control value at $P \leq 0.01$.

Table (6): Effect of Lead Acetate Exposure Via Drinking Water Administration on Iron, Zinc, Copper, Manganese Levels, and Lead Residues in Different Organs of F_1-Male Mice.

Gossmating Groups	Mean Metal Concentrations-ug/g wet tissue ±SD				
	Fe	Zn	Cu	Mn	Pb
			Liver		
1[a]	91.66±8.1	42.60±12.98	1.68±0.46	0.63±0.08	0.15±0.04
2[b]	98.03±6.81	49.88±12.7	1.66±0.20	0.63±0.09	0.43±0.71*
3[c]	98.36±7.41	47.80±10.4	1.69±0.38	0.59±0.17	0.41±0.14*
4[d]	91.44±8.6	49.80±12.6	1.61±0.42	0.53±2.6	0.15±0.09
5[e]	93.50±25.5	47.78±11.3	1.69±0.49	0.59±0.19	0.20±0.3
6[f]	98.20±30.9	44.10±6.34	1.69±0.42	0.47±0.19	0.12±0.05
7[g]	92.56±8.0	44.80±11.0	1.67±0.5	0.14±0.21	0.19±0.28
			Kidney		
1[a]	134.79±24.8	7.75±2.1	4.38±2.4	2.54±1.0	0.11±0.00
2[b]	148.37±14.5	8.00±1.7	3.19±1.7	2.11±1.9	0.12±0.02
3[c]	145.10±28.2	6.90±1.5	4.00±1.8	2.90±1.5	0.11±0.0
4[d]	146.60±13.9	7.03±1.4	5.29±2.3	2.29±0.3	0.15±0.1
5[e]	169.5±18.4	6.03±1.0	3.16±0.7	3.35±1.5	0.12±0.0
6[f]	128.7±27.5	7.30±1.0	4.32±1.3	2.76±0.3	0.13±0.05
7[g]	122.3±47.8	7.11±1.7	4.55±1.4	2.21±1.4	0.12±0.3

	Brain				
1[a]	69.12±7.77	5.59±0.9	4.47±0.9	2.72±0.6	0.30±0.2
2[b]	65.48±7.7	5.71±0.6	4.28±1.3	2.24±0.7	0.37±0.19
3[c]	70.53±16.0	6.40±0.7	4.00±1.6	2.94±1.37	0.32±0.1
4[d]	66.95±5.04	6.74±0.7	6.74±1.1	6.74±1.1	0.31±0.0
5[e]	68.54±6.4	6.61±0.48	6.61±0.48	2.68±0.7	0.33±0.03
6[f]	73.44±12.9	7.83±0.9	4.52±1.1	3.22±1.2	0.31±0.02
7[g]	75.47±6.8	7.40±1.3	5.92±2.8	4.08±1.9	0.35±0.03

Note: lead acetate concentrations (%).

[a]Control female x control male, [b]Control male x 0.26% lead acetate female, [c]Control male x 0.026% lead acetate female, [d]Control female x 0.026% lead acetate male, [e]Control male x 0.0026% lead acetate female, [f]Control female x 0.0026% lead acetate male, and [g]0.0026% lead acetate male x 0.0026% lead acetate female.

***Significantly different from control value at $P \leq 0.05$.**

source of fetal lead exposure (maternal and fetal blood lead levels are nearly equivalent and 10 times as high as the corresponding blood lead levels in milk) (Ong *et al*., 1985, Watson *et al*., 1997). Indeed, lead levels in the breast milk tend to increase over extended lactation (Bonithon-Kopp *et al*., 1986, Hallen *et al*., 1996, Watson *et al*., 1997) Lead is also excreted in human milk in concentrations as high as 12 µg/L (Murthy and Rhea, 1971). In addition pregnancy, as a condition of calcium stress, may induce changes in bone physiology and mineral metabolism that result in mobilization of lead from bone stores back into maternal circulation and back into fetal tissues (Silbergeld 1991)

The body burden of lead during childhood increases with age (kammholz *et al*., 1972). Lead concentration in blood rises immediately after the first inhalation exposure and levels off after a month of occupational exposure (Tola *et al*., 1973). Ninety percent of the blood-borne lead is bound to erythrocytes (Six and Goyer 1970). Triphasic elimination of lead from blood has been observed , clearance with half - times from 35-40 days mainly represents the washout from softy tissues; half - times of 6 months and 20 years mainly represent the washout from the skeleton (Piotrowski 1971).

The correlation between lead concentrations in tissues and clinical observation is affected by duration of increased lead concentrations in tissues. Stankovic 1971 considered concentrations below 60 µg/100 ml non effective levels There may be as increase in risk in the female compared to the male (Bridbord 1978, Zlelhuls 1978). The World Health Organization (WHO) recommended a health-based biological exposure limit of 40 ug/100 ml in the blood of males and females over the reproductive age and below 30 µg/ml for females in the reproductive age (WHO, 1980)

In summary, this study had shown that lead acetate exposure via drinking water in the premated male and female mice, postamted male mice, females after gestation and lactation periods, F_1-generation associated with alterations in disposition of Fe, Zn, Cu, and Mn It is

suggested that these changes, may be responsible in part for the adverse reproductive outcomes commonly associated with lead exposure during pregnancy in animals.

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الملخص العربى

تأثير التداخل بين الرصاص والعناصر الصغرى الرئيسيه خلال الجيل الأول لفئران التجارب

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تم تصميم هذه التجربه لدراسة تأثير عنصر الرصاص على تركيز عناصر الحديد والزنك والنحاس والمنجنيز فى الكبد والكليه والمخ للأمهات والآباء والجيل الأول لفئران التجارب. بجانب تقدير نسبة الرصاص الموجوده فى نفس الأعضاء السابقة. تم تعريض اناث وذكور الفئران للتركيزات الآتيه من خلات الرصاص فى مياه الشرب 0.26، 0.026، 0.0026% (14.2، 142، 1420 جزء فى المليون من الرصاص) لمدة 70 يوم. بالإضافه إلى إجراء تجارب التزاوج العكسى لإنتاج الجيل الأول.

وأوضحت النتائج أن تركيز الرصاص فى الكبد والكليه والمخ يقل أثناء فترة الحمل والرضاعه مقارنة بفترة ما قبل الحمل. أيضا نسبة الرصاص فى نفس الأعضاء تناقصت فى الذكور بعد التزاوج عنه قبل التزاوج. وكذلك فإن التغيرات الموجوده بالنسبه لتركيز النحاس والزنك والمنجنيز والحديد فى الأعضاء تحت الدراسة لإناث وذكور الفئران قبل التزاوج تكون مماثله لتركيزاتها بعد التزاوج وبعد الحمل والرضاعه.

لم تتأثر مستويات هذه العناصر فى إناث الجيل الأول لكل مجاميع الـــتزاوج فـــى الكليه والمخ مقارنه بالكنترول وذكور الجيل الأول. يوجد فرق معنوى بين مستوى الرصـلص المتبقى فى الكبد والمخ والكلية للجيل الأول لإناث الفئران الناتجه من بعض مجاميع الـــتزاوج مقارنه بالجيل الأول للكنترول. يوجد ارتفاع معنوى فى نسبة الرصاص المتبقى فى كبد ذكور الجيل الأول فى بعض مجاميع التزاوج مقارنة بالكنترول.