

# Lead Induced Morphological Changes in Cerebral Cortex of Albino Mice: An Experimental Study

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## ABSTRACT

This experimental study was designed to see the possible effects of lead on brain morphology of albino mice. For this purpose, sixty albino mice were selected and divided into five groups. Group 0 was scarified after first week for baseline morphology. Group I, (normal control) was fed on synthetic diet, group II, III and IV were given lead acetate 2 mg, 4 mg and 8 mg/kg/day respectively for 60 days. Histological examination was done on H&E and Rhodizonate methods. Cerebral cortex of albino mice revealed increased oedema, congestion and neuronal changes (pyknosis) in group II (mice with lead dose 2 mg/kg/day). Group III and IV showed moderate changes in all the parameters of cerebrum of albino mice. Rhodizonate stain did not show lead deposition in mice cerebral cortex at these blood lead levels. It is concluded that brain is one of the sensitive organs to low levels of lead toxicity.

**Key words:** Cerebral Cortex, Lead

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## INTRODUCTION

Lead is a naturally occurring element that had been widely used in industry and in agriculture (Pesticide). Humans are in contact with this since the recorded history of mankind<sup>1</sup>. Lead poisoning is an environmental disease that occurs throughout the world<sup>2</sup>. Certain professions such as news printers<sup>3</sup>, bus driver<sup>4</sup>, battery factory workers<sup>5</sup> and lead smelters are more exposed and affected by lead poisoning. Many industrial activities and particularly its use in petrol (gasoline)<sup>6</sup> have led to its wide distribution so that all humans have lead in their bodies. The average level of lead in general population is approximately 2.8 micro-gram/dl<sup>7</sup>.

Lead is distributed in the body in blood (1 % of the body lead burden), soft tissue e.g. kidneys and nervous system and skeleton (95% of the body lead in adults and 70% in children). Lead in blood has an estimated half life of 35 days, in soft tissue 40 days and in bones 20 to 30 years<sup>8</sup>. Lead is mainly excreted in urine and in faeces<sup>6</sup>. Lead also appears in hairs, nails, sweats, saliva and breast milk<sup>9</sup>. Lead is a toxic agent and serves no known beneficial role in the human body<sup>10</sup>.

In acute cases of lead poisoning, the brain is extremely edematous and microscopically, necrosis of cerebral and cerebellar white matter may occur, followed by diffuse astrocytic proliferation. There is also endothelial proliferation of small capillaries of the

It has been reported that Vitamin c, if taken in regular doses, have potential for reducing accumulated lead from human body<sup>13</sup>. Lead exposure in childhood lowers IQ scores. Because IQ, per se, affects behavior, measuring the direct effect of lead concentration, usually at 2 years old, or the lower blood lead level measured at school age may be the most relevant<sup>14</sup>.

## MATERIAL & METHODS

In this experimental study, sixty albino mice were selected. At zero week, twelve mice were dissected to provide base line control. Remaining 48 mice were divided in four groups, each having 12 mice. Group-I served as control throughout the study. Groups II, III and IV were given lead acetate in deionized water through Oral intubation for sixty days. The doses of lead acetate were 2, 4 and 8 mg/kg/day (or) .002, .004 and .008 mg/gm/day in group II, III and IV respectively<sup>15</sup>. The blood sample was taken by heart puncture. Blood was collected in a glass container having EDTA. After taking blood samples, animal was anesthetized till death. Brain was exposed and dissected out.

## RESULTS

Blood lead levels and morphological changes of cerebrum in different groups of albino mice were given in tables 1 and 2.

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Table 1: Comparison of blood lead level between control (i) and experimental group II, III &amp; IV at 60 days

Blood Lead Levels	I (Control)	II	III	IV
Mean $\pm$ SD Value	0.217 $\pm$ 0.013	0.247 $\pm$ 0.019	0.410 $\pm$ 0.020	0.662 $\pm$ 0.024
Ranges	0.2 – 0.236	0.226 – 0.278	0.386 – 0.432	0.626 – 0.691
Total	12	12	12	12

Statistical Analysis: I vs II = p > 0.05 (NS) I vs III = P < 0.05 (S) I vs IV = P < 0.01 (HS)

Table 2: Cerebral changes in different groups

Microscopic Features	No. of animals with positive changes			
	Group I	Group II	Group III	Group IV
Oedema	0	08	11	12
Necrosis	0	02	10	11
Astrocytic Proliferation	0	02	11	11
Endothelial Proliferation	0	01	11	11
Congestion	0	10	12	12
Pyknosis	0	09	11	12

Key: Group I = Synthetic Diet  
 II = Lead dose 2 mg/kg/day  
 III = Lead dose 4 mg/kg/day  
 IV = Lead dose 8 mg/kg/day

## DISCUSSION

**Blood lead levels:** In the present study, the blood lead levels in the control groups were not significantly different at different time intervals. On the other hand, doubling of blood lead levels between 2 and 4 mg/kg/day dose groups and failure to observe a similar increase between 4 and 8 mg/kg/day groups may be explained by the fact that relative blood lead levels are not linearly correlated with the dose administered<sup>15</sup>. It is suggested that mechanisms responsible for lead absorption might get saturated if large single doses are administered. It is in agreement with the study done by Viskocil et al (1995)<sup>16</sup> about cerebral hemispheres in mice following lead exposure.

**Comparison of Group II (lead dose 2 mg/kg/day) with control group I:** The microscopic findings in cerebrum of albino mice regarding Oedema, congestion and pyknosis were significant when compared with control group (p = 0.0062, p = 0.0062 and p = 0.0012 respectively). These findings are in agreement with the results of Anttila et al (1996)<sup>17</sup> Michaels et al (1991)<sup>3</sup> and Nowack et al (1993)<sup>18</sup>.

**Comparison of Group III (mice with lead dose 4 mg/kg/day) with control group I:** Microscopic features of cerebrum regarding Oedema, necrosis, astrocytic proliferation, vascular changes and neuronal changes showed mild to moderate type of histological changes as compared to control group. The difference was statistically significant in above mentioned histological parameters. These findings are consistent with the results of Logdberg et al (1988)<sup>19</sup>, Harry et al (1996)<sup>20</sup> Anttila et al (1996)<sup>17</sup>, Michaels et al (1991)<sup>3</sup> and Nowack et al (1993)<sup>18</sup>.

**Comparison of Group IV (mice with lead dose 8 mg/kg/day) with control group I:** Microscopic features of cerebrum regarding Oedema, necrosis, astrocytic proliferation, endothelial proliferation, congestion, and neuronal changes (pyknosis) showed moderate type of histological changes as compared to control group (I). The difference was significant statistically in above mentioned parameters. These findings are consistent with the results of Anttila et al (1996)<sup>17</sup>, Michaels et al (1991)<sup>3</sup> and Nowack et al (1993)<sup>18</sup>.

## REFERENCES

1. Rojas E, Herrera LA, Poirier LA, Ostrosky WP. Are metals dietary carcinogens? *Mutat Res* 1999; 443:157-81.
2. Hsieh LL, Liou SH, Chen YH, Tsai LC, Ynag T, Wu TN. Association between aminolevulinic dehydrogenase genotype and blood lead levels in Taiwan. *JEOM* 2000; 42: 151-5.
3. Michaels D, Zoloth SR, Stern FB. Does low level lead exposure increase risk of death. A mortality study of newspaper printers. *Int J Epidemiol* 1991; 20:978-83.
4. Sharp DS, Osterich J, Becker CE, Bernard E, Smith AI-1, Fisher JM, et al. Blood pressure and blood lead concentration in bus drivers. *Environ Health Perspect* 1989; 78 131-7.
5. Grandjean P, Jenson BM, Sando SH, Jordensen PJ, Antonsen S. Delayed blood regeneration in lead exposure. An effect on reserve capacity. *Am J Pub H* 1989; 79:1385-7.
6. Hu H payton M, Korrick S. Determination of bone and blood levels among community-exposed middle aged to elderly men. *Am J Epidemiol* 1996; 144:749-59.
7. Sokas R, Schwartz E, Wesdock JC. Occupational Lead poisoning. *Am Fam Physician* 1998; 57:719-26.

8. Grimsley EW, Adams M.L. Occupational lead intoxication: Report of four cases. *South Med J* 1994; 87:689-91.
9. Saleh IA, Mustafa A, Dufoour L, Jaylor A, Hiton R. Lead exposure in the city of Arar Saudi Arabia. *Arch Env* 1996; 51:73-82.
10. Schwartz .I. Lead blood pressure and cardio vascular disease in men. *Arch Env 1-J* 1995;50:31-7
11. Hennigar GR. Drug and Chemical injury - Environmental Pathology. In Kissane JM, (ed). *Anderson's Pathology*. 9<sup>th</sup> Ed. Philadelphia: CV Mosby Company 1990: 146-239.
12. Aw TC, Vale TA. Poisoning from metals. In: Weatherall DJ, Ledingham JGG, Warrell DA eds. *Oxford Textbook of Medicine*. 3<sup>rd</sup> Ed. New Jersey: Oxford University Press 1996: 1105-15.
13. Khawaja MA. Environmental health: Lead exposure & its impacts on children, *environmental Health*, 2003; 10 (2); 1-4
14. Chen A, Cai B, Dietrich KN, Radcliffe JWJ. Lead Exposure, IQ, and behavior in Urban 5 to 7 year olds: Does Lead affect behavior only by lowering IQ. *Pediatrics* 2007; Vol. 119 (3).
15. Junaid M, Choudhuri DK, Naryan R, Shanker R, Saxena DK. Lead induced changes in ovarian follicular development and maturation in mice. *J Toxicol-Env H* 1997;50:31-40.
16. Viskocil A, Semecky V, Faila Z, Cizkova M, Viau C. Renal alteration in female rats following subchronic . Lead exposure. *J Appl Toxicol* 1995; 15 (4): 257 – 62.
17. Anttila A, Heikkila P, Nykyri E, Kaupeinen T, Pukkola E, Lernberg S et al. Risk of nervous system cancer among workers exposed to lead. *JEOM* 1996; 38:131-6.
18. Nowack R, Wiecek A, Exner B, Gretz N, Ritz E. Chronic lead exposure in rats. Effects of blood pressure. *Eur J Clin Invest* 1993; 23:203-206.
19. Logdberg B, Burn A, Berlin M, Schutz A. Congenital lead encephalopathy in monkeys. *Acta Neuropathol Berl* 1988; 77(2):120-7.
20. Harry GJ, Schmitt TJ, Gong Z, Brwon H, Zawia N, Evans HI. Lead induced alterations of glial Fibrillary acidic protein in the developing rat brain. *Toxicol Appl Pharmacol* 1996 Jul;139(1): 84-93.