Tissue Disposition of ^{54}Mn in Lead Pretreated Rats

Key words : Lead— ^{54}Mn —Brain—Liver—Blood

During clinical investigations emphasis is generally placed on the study of a single toxic agent and, therefore, the knowledge regarding the implications of possible interactions between xenobiotics and their effect on human health has remained fragmentary. Industrial workers and the general population, over-exposed to lead (Pb) in the work environment or through polluted biosphere, may also be exposed to other elements, both essential and nonessential. Zielhuis *et al.*¹⁾ reported increased blood manganese (Mn) levels with increased blood Pb in young children and occupationally exposed workers. Studies reported from our laboratory have shown significant alterations in neurochemical and behavioral profile of animals coexposed to Mn and Pb.²⁾ These results suggested a close relationship between Pb and Mn metabolism. In the present investigations we have, therefore, studied the distribution of ^{54}Mn in various tissues of Pb exposed animals so as to understand the mechanism of Pb and Mn interaction in the biological system. Two doses of Pb have been used to study the dose-response relationship on the distribution pattern of ^{54}Mn in tissues.

Adult male rats were randomly divided into three groups of 6 animals each. Animals of groups I and II were given lead acetate (Pb 30 and 300 ppm, respectively) through drinking water, *ad libitum* while those of group III received an equimolar solution of sodium acetate in the same manner and served as controls. After 90 days of Pb treatment, ^{54}Mn (10 μCi per rat of approximately 200 g body weight) was administered intraperitoneally to all the rats. Sixty minutes after injection all the animals were sacrificed for studying the distribution of ^{54}Mn in various tissues by using LKB ultra 1280 Gamma counter. Significance of data was evaluated by Students 't' test and values less than 0.05 were considered significant.

Table 1 shows that the administration of Pb at a dose of 30 ppm and 300 ppm significantly decreased the weight of pancreas while 300 ppm reduced the weight of the testis. There was no change in the weight of liver, brain, bone, lungs, heart, kidney and spleen after administration of Pb.

Table 2 shows that 50% of ^{54}Mn administered was recovered in liver tissue in control animals. It is also interesting to report that the pancreas which was 10 times less in mass as compared to liver showed about 3% of ^{54}Mn concentration. In the same animals, the concentration of ^{54}Mn in kidney and spleen was 1.4% and 0.9%, respectively. Significant amount of ^{54}Mn was also observed in testes. Heart, lungs, bone and brain showed only measurable amount of radioactivity. This is in accordance with the earlier observations of wide distribution of manga-

Table 1. Absolute organ weights of rats exposed to Pb (30 ppm and 300 ppm) through drinking water

Tissue	Control	Pb 30 ppm	% change	Pb 300 ppm	% change
Pancreas—(g)	0.6457±0.0265	0.4973±0.0195 p<0.01	-23	0.4267±0.0186 p<0.001	-34
Testis—(g)	2.7264±0.2351	2.5024±0.2272 N.S.	Nil	1.7968±0.1282 p<0.01	-34

Data represent mean±S.E. of five rats; values of p evaluated by Students 't' test; (-) Decrease; N.S.—Not significant.

Table 2. Distribution of ⁵⁴Mn in various tissues of rat treated with 30 ppm and 300 ppm of Pb

Tissues	Per cent distribution of ⁵⁴ Mn per g of wet tissue				
	Control	Pb 30 ppm	% change	Pb 300 ppm	% change
Liver	7.625 ±0.339	5.551 ±0.291 p<0.001	-27	4.746 ±0.248 p<0.001	-38
Brain	0.0356±0.0022	0.0389±0.0024 N.S.	Nil	0.0534±0.0039 p<0.01	+50
Blood*	0.0732±0.0081	0.0556±0.0023 N.S.	Nil	0.1573±0.0196 p<0.01	+115
Bone**	0.0661±0.0062	0.0609±0.0033 N.S.	Nil	0.1003±0.0078 p<0.01	+52
Lungs	0.175 ±0.0082	0.194±0.017 N.S.	Nil	0.400 ±0.016 p<0.001	+129
Testis	0.187 ±0.0257	0.422 ±0.324 N.S.	+126	0.455 ±0.0528 p<0.001	+138
Heart	0.435 ±0.046	0.389 ±0.025 N.S.	Nil	0.599 ±0.038 p<0.05	+38
Kidney	1.075 ±0.067	1.123 ±0.095 N.S.	Nil	1.681 ±0.158 p<0.01	+56
Spleen	2.073 ±0.243	2.275 ±0.274 N.S.	Nil	2.325 ±0.303 N.S.	Nil
Pancreas	4.618 ±0.905	4.156 ±0.767 N.S.	Nil	4.819 ±0.595 N.S.	Nil

Data represent mean±S.E. of five rats; Values of p evaluated by Students 't' test; (+) Increase; (-) Decrease; N.S.—Not significant

* Per ml blood

** Femur only

nese throughout the body tissues with highest accumulation in liver, pancreas, kidney and pituitary gland, which are rich in mitochondria.³⁾

The distribution of ⁵⁴Mn in various organs of rats exposed to 30 ppm and 300 ppm of Pb is also given in Table 2. The data indicated 126% increase in the radioactivity in testes, the increase was more marked in the rats treated with 300 ppm of Pb. However, ⁵⁴Mn concentration decreased in liver by 27% and 38% in animals treated with 30 ppm and 300 ppm of Pb, respectively. At the low dose level, the radioactivity remained unaffected compared to that observed in animals treated with ⁵⁴Mn only. However, there was no change in ⁵⁴Mn

contents in spleen and pancreas at either dose level of Pb, while Pb pretreatment at a dose of 300 ppm produced significant increase in the accumulation of ^{54}Mn in the blood, testes, bones, brain, kidney and heart.

Increased retention and redistribution of one metal in the presence of another metal has been reported by several investigators.^{4,5)} Coadministration of selenium and mercury have been found to increase the retention of both the metals and also caused a redistribution of mercury in the organs,⁶⁾ in the blood⁷⁾ and diversion from low molecular weight to high molecular weight proteins. In the present experiment, Pb pretreatment produced significant alterations in the tissue distribution pattern of ^{54}Mn , in most of the tissues the alterations were dependent on the dose of Pb. Significant decrease in the accumulation of ^{54}Mn in the liver of Pb pretreated rats may be due to the saturation of cellular receptor sites by previous Pb binding. Decrease in ^{54}Mn concentration in the liver of Pb pretreated rats with greater magnitude of alteration at high dose level is of significance since liver regulates the excretion of manganese mainly through the biliary passages.⁸⁾ Decreased excretion of ^{54}Mn through this passage in Pb pretreated rats may be responsible for significant increase in the radioactivity in brain, blood, lungs, kidneys and testes of these animals. Therefore, the presence of Pb in the body-interferes with the homeostasis of manganese which is generally regulated by excretion rather than absorption.⁹⁾ Thus, significant changes in manganese homeostasis in Pb exposed animals may be responsible for altered biological response after coexposure to manganese and Pb.

REFERENCES

- 1) Zielhuis, R. L., Castilho Pdel, Herber, R. F. M. and Wibowo, A. A. E. (1978). Levels of lead and other metals in human blood: suggestive relationship, determining factors. *Environ. Health Perspect.*, **25**, 103.
- 2) Chandra, S. V., Ali, M., Saxena, D. K. and Murthy, R. C. (1981). Behavioral and neurochemical changes in rats simultaneously exposed to manganese and lead. *Arch. Toxicol.*, **49**, 49.
- 3) Maynard, L. S. Cotzias, G. C. (1955). The partition of manganese among organs and intracellular organelles of the rat. *J. Clin. Invest.*, **35**, 831.
- 4) Underwood, E. J. (1979). Interactions of trace elements: In: *Toxicology of Heavy Metals in the Environment* (Edited by F. E. Oehme), Part 2, 64. Marcel Dekker Inc., New York Basel.
- 5) Malhotra, K. M., Shukla, G. S. and Chandra, S. V. (1982): Neurochemical changes in rats coexposed to lead and copper. *Arch. Toxicol.*, **49**, 331.
- 6) Chen, R. W., Whanger, P. D. and Fang, S. O. (1974). Diversion of mercury binding in rat tissues by selenium: A possible mechanism of protection. *Pharmacol. Res. Commun.*, **6**, 511.
- 7) Burk, R. F., Foster, K. A., Greenfield, P. M. and Kiker, K. W. (1974). Binding of simultaneously administered inorganic selenium and mercury to rat plasma protein. *Proc. Soc. Exp. Biol. Med.*, **145**, 782.
- 8) Papavasiliou, P. S., Miller, S. T. and Cotzias, G. C. (1966). Role of liver in regulating

distribution and excretion of manganese. *Am. J. Physiol.*, **211**, 211.

- 9) Britton, A. A. and Cotzias, G. C. (1966). Dependence of manganese turnover on intake. *Am. J. Physiol.*, **211**, 203.

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