

## COMPARATIVE METABOLISM OF HIGH LEAD DOSE LEVELS IN SUCKLING AND ADULT RATS

B. MOMČILOVIĆ

*Institute for Medical Research and Occupational Health, Yugoslav Academy  
of Sciences and Arts, Zagreb*

*(Received for publication April 18, 1974)*

The kinetics of lead distribution and retention was studied in 15 and 120 day-old rats after a single intraperitoneal application of 500  $\mu\text{g}$  Pb/kg body weight labelled with tracer amount of  $^{203}\text{Pb}$ . After eight days the percentage  $^{203}\text{Pb}$  retention was about eight times higher in the brain, twice higher in the femur and liver and half as high as in the whole blood and teeth, but two times lower in the kidneys in sucklings as compared to adults. These differences are in agreement with our previous studies on the kinetics of tracer doses of lead in young and adult rats. The higher lead dose level used in this experiment caused a higher percentage of lead retention and a slower lead elimination in tissues of both suckling and adult rats.

The impact of environmental lead contamination on human health as well as increased risk of lead poisoning in the very young is well documented (1, 2, 3, 4). In our previous work we were able to demonstrate some marked differences in the kinetics of the retention and distribution of tracer doses of lead in suckling as compared to adult rats (5). The aim of our present work was to examine and compare the kinetics of retention and distribution after giving high doses of lead to suckling and adults rats.

### MATERIALS AND METHODS

The experimental technique used was essentially the same as in our previous work (5).

Experiments were performed on 15- and 120-days-old female albino rats. The 15-day old suckling rats were in a litter of six together with

their mothers. All adult animals were fed a stock laboratory diet (1.2% Ca and 0.8% P) with water *ad lib*.

All experimental animals received a single intraperitoneal injection of 50  $\mu\text{Ci}$   $^{203}\text{Pb}$  with addition of 500  $\mu\text{g}$  Pb as acetate in a volume of 5 ml per kg body weight. In each litter one out of six baby rats was injected to avoid cross contamination. Lead-203 in an almost carrier free form was supplied by the Gustaf Werner Institute, Uppsala, Sweden. The whole body gamma ray activity of each animal was determined in a single channel twin crystal assembly (Tobor, Nuclear Chicago) at 6, 12, 24, 48, 72, 96, 120, 144, 168, and 192 hours after application of the marker.

Some adult and suckling animals were sacrificed by exsanguination in ether anaesthesia at 24, 72, 144, and 192 hours after the injection of the marker. Liver, both kidneys, whole brain, femur and four incisor teeth were dissected and their wet weight determined immediately after removal. The whole blood collected from the abdominal aorta was weighted without addition of anticoagulants and the volume was corrected for the theoretical blood volume in rats (6). The results were expressed for the total blood. The tissues and blood were placed into round aluminium planchettes and  $^{203}\text{Pb}$  activity was determined in a single channel crystal assembly (Well, Nuclear Chicago).

The results are expressed as percentages of the injected dose and presented as the arithmetic mean with the standard error of the mean. Statistical data processing consisted also in calculating the regression lines as logarithms of the percentage of lead-203 dose ( $y$ ) versus logarithms of time in hours ( $x$ ), i. e.  $\log y = a + b \log x$ . The difference between the arithmetic means of the percentage of the dose as well as the differences between the slopes ( $b$ ) and intercepts ( $a$ ) of regression lines were tested by means of Student's  $t$ -test and the significance of the slopes of the regression lines was tested by the correlation coefficient.

## RESULTS

The whole body retention was much higher in sucklings than in adult rats (Table 1). After an eight-day period there was still about 85% of injected dose left in the sucklings as compared to about 56% in adult animals.

The  $^{203}\text{Pb}$  retention in tissues and its variations with time are presented in Table 2 for both suckling and adult rats. After 24 hours the highest percentage for adult animals was found in liver (7.2%) and in decreasing order in the kidneys (4.9%), whole blood (2.0%), femur (0.38%), teeth (0.26%) and brain (0.02%). This order was a little different in sucklings with the highest retention again in the liver (7.2%), but higher in the whole blood (1.8%) than in kidneys (0.8%). Further the order was the same for femur (0.58%), teeth (0.28%) and brain (0.11%). After 192 hours the percentage of  $^{203}\text{Pb}$  retained in the tissues of sucklings as compared



Table 1

<sup>203</sup>Pb in the whole body of suckling and adult rats after a single intraperitoneal injection expressed as per cent dose

Hours after application	Sucklings	Adults
1	98.35 ± 1.32* (25)**	99.65 ± 0.58 (18)
6	96.53 ± 1.82 (13)	98.59 ± 0.67 (10)
12	96.03 ± 1.80 (13)	96.22 ± 0.48 (10)
24	94.52 ± 1.17 (25)	92.22 ± 0.71 (17)
48	92.67 ± 1.95 (13)	83.43 ± 0.98 (10)
72	92.32 ± 1.11 (25)	76.85 ± 1.19 (18)
96	91.14 ± 1.98 (13)	71.68 ± 1.53 (10)
120	91.20 ± 1.83 (13)	66.29 ± 1.69 (10)
144	87.84 ± 1.42 (25)	61.92 ± 1.23 (18)
168	86.85 ± 1.84 (13)	59.20 ± 1.60 (10)
192	84.80 ± 1.21 (27)	56.24 ± 1.24 (17)

\* Mean ± SE

\*\* The number of samples

Table 2

<sup>203</sup>Pb in tissues of suckling and adult rats after a single intraperitoneal injection expressed as per cent dose

Hours after application	No of rats	Sucklings					
		Whole blood	Liver	Kidneys	Brain	Femur	Inci-sors
24	12	1.77*	7.16	0.76	0.109	0.58	0.28
		0.32**	0.88	0.04	0.008	0.03	0.02
72	12	1.08	4.32	0.77	0.138	1.14	0.55
		0.12	0.81	0.04	0.013	0.09	0.06
144	12	1.19	3.73	0.87	0.143	1.32	0.76
		0.06	1.01	0.07	0.009	0.08	0.04
192	14	1.16	4.04	0.82	0.177	1.64	1.03
		0.07	0.83	0.04	0.013	0.09	0.08
Adults							
24	6	1.99	7.20	4.88	0.015	0.38	0.26
		0.19	0.79	0.37	0.002	0.05	0.04
72	8	1.49	4.86	3.62	0.021	0.60	0.45
		0.08	0.41	0.23	0.002	0.03	0.04
144	8	0.91	2.97	1.94	0.019	0.79	0.61
		0.07	0.46	0.13	0.002	0.06	0.05
192	7	0.73	2.52	1.69	0.021	0.88	0.77
		0.04	0.41	0.08	0.001	0.04	0.04

\* Mean

\*\* SE of the mean

with adults was about eight times higher in brain (0.18% v. s. 0.02%), about twice higher in femur (1.64% v. s. 0.88%) and liver (4.04% v. s. 2.52%), one and a half times greater in the whole blood (1.16% v. s. 0.73%) and teeth (1.03% v. s. 0.77%), but two times lower in kidneys (0.82% v. s. 1.69%).

It is seen from Table 2 that  $^{203}\text{Pb}$  elimination from the liver and whole blood was much slower in sucklings than in adults. The retention of the lead marker in the kidney of the sucklings remained unchanged while that in adults slowly decreased. Also the retention of  $^{203}\text{Pb}$  in the brain, femur and teeth of the sucklings increased markedly over the 8-day experimental period while that in adults was lower and showed comparatively smaller changes with time.

The statistical treatment of data presented in Table 2 is shown in Figures 1—6 in the form of regression lines.

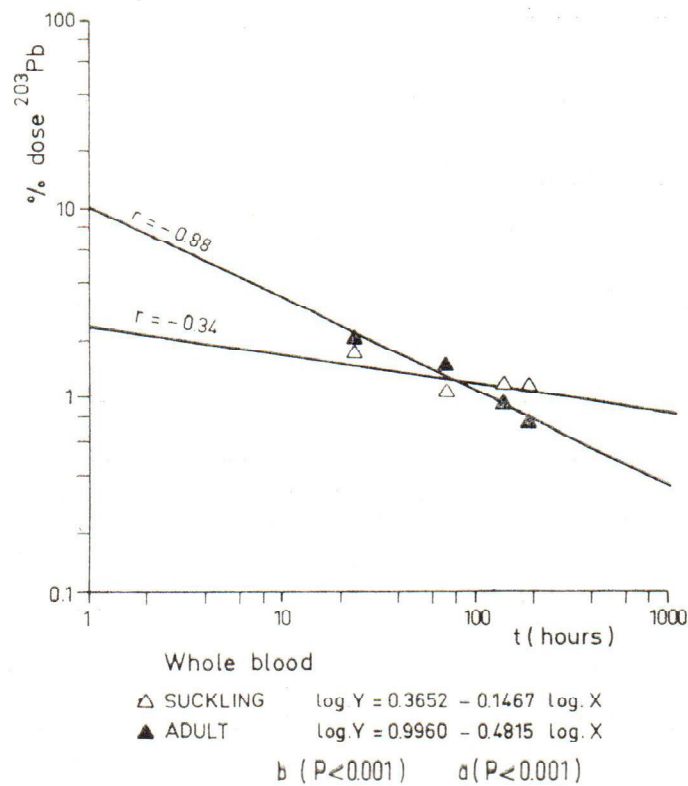


Fig. 1. Kinetics of lead retention in the whole blood

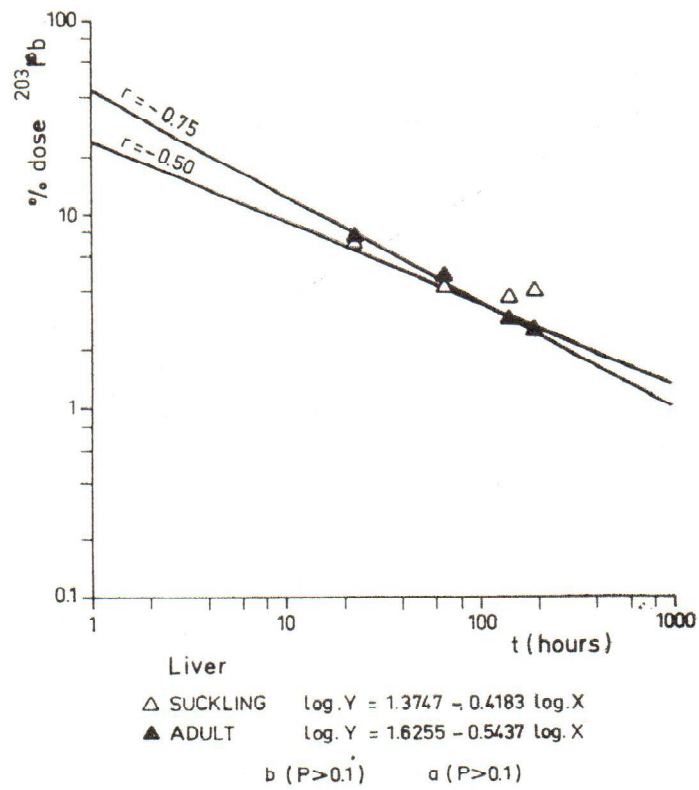


Fig. 2. Kinetics of lead retention in the liver

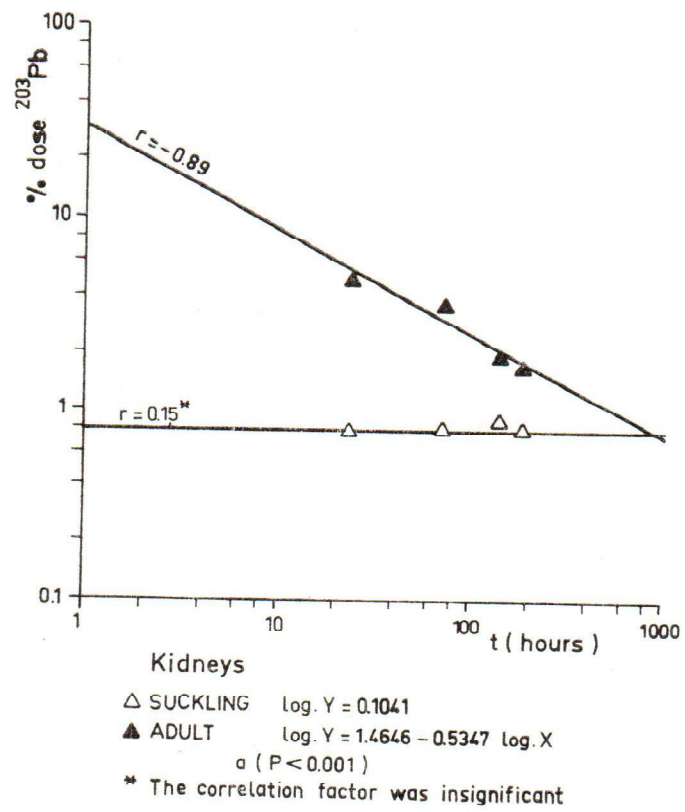


Fig. 3. Kinetics of lead retention in the kidneys

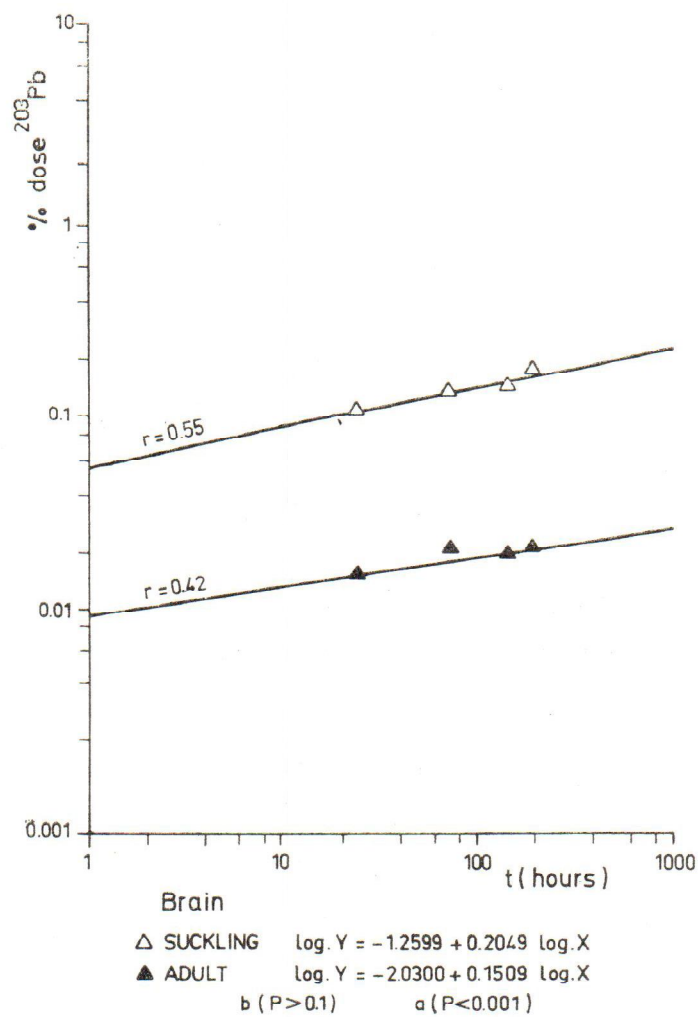


Fig. 4. Kinetics of lead retention in the brain

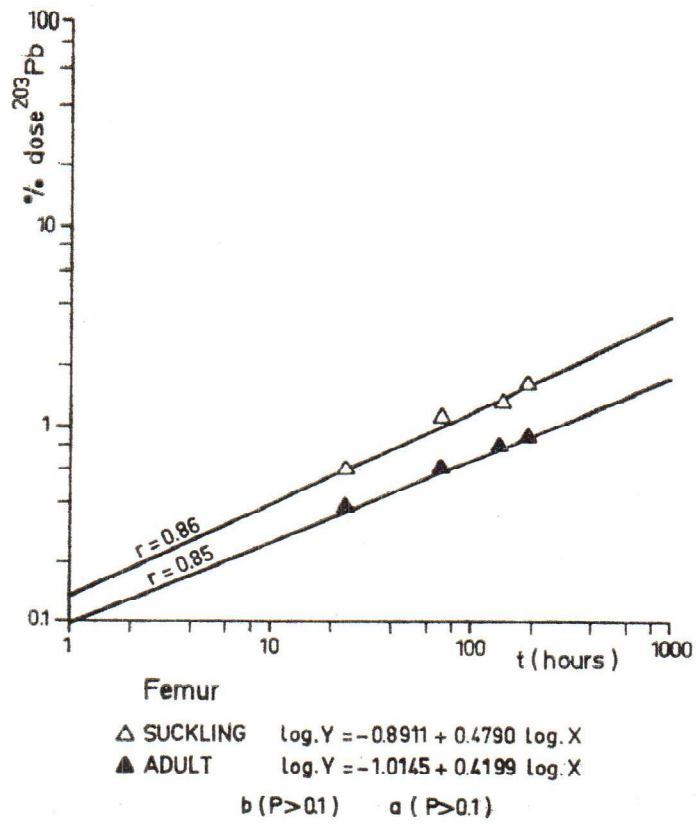


Fig. 5. Kinetics of lead retention in the femur



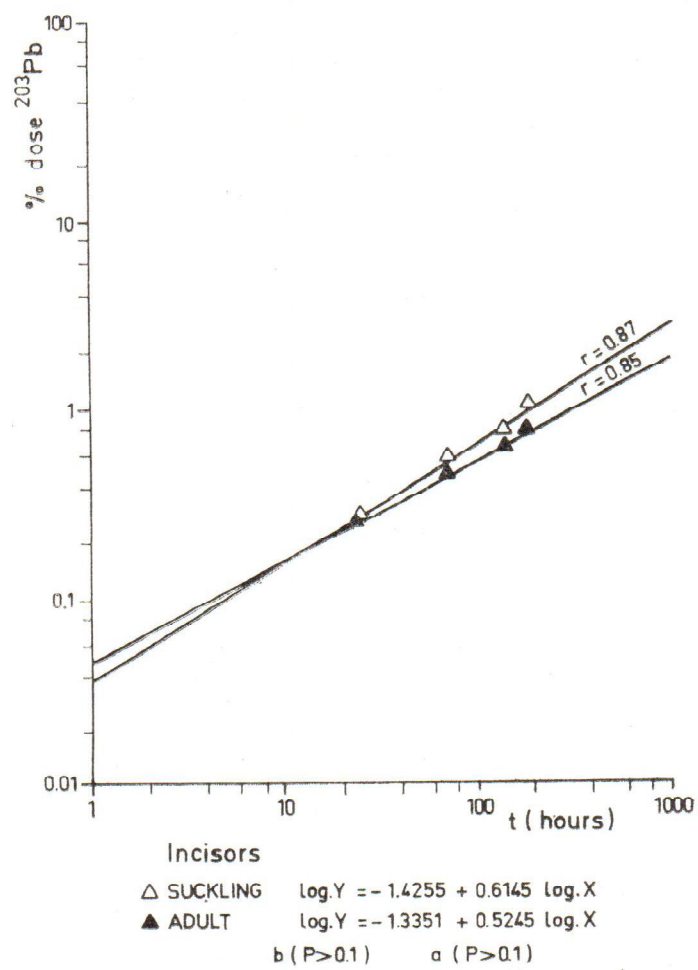


Fig. 6. Kinetics of lead retention in the incisors

## DISCUSSION

The results of this experiment confirm our previous finding about higher retention and slower elimination of lead from various tissues in suckling as compared to adult rats (5). The higher lead dose level used in this experiment was accompanied with a slower elimination rate from the whole blood, liver and kidneys and a higher deposition rate in the brain, femurs and teeth as compared with the trace dose levels of lead used in our previous work.

The results of whole body retention in adults are in good agreement with those of *Castellino* and *Aloj* (7) and *Bolanowska* and *Piotrowski* (8), while the lead-203 retention in the tissues was higher than in our experiments. This may be attributed to the difference in age and sex as well as to a different route of administration of the marker. However, the slopes of our regression lines were in good agreement with the results of *Teisinger* et al. (9), although they used rabbits and determined the tissue lead content over many days after animals finished receiving a lead containing diet.

The higher ability of young tissues to bind lead may be attributed to many factors i. e. higher phosphate content of juvenile plasma, higher body and extracellular water content in young organisms which were extensively reviewed in our previous paper (5). The slower elimination rate and higher deposition rate of high as compared to tracer dose levels of lead for both suckling and adult rats are in good agreement with a well known fact that lead is a cumulative poison (1) but physiological significance of this phenomenon is still obscure.

A previous report from this laboratory of a very high lead absorption from the intestinal tract of newborn rats (10) together with the results of a much higher retention of trace (5) and high lead dose levels in the whole body and tissues of sucklings as compared to adults may partly explain the outstanding susceptibility to lead of the young.

## References

1. *Hammond, P. B.*: Essays in toxicology, 1 (1969) 115.
2. *Barltrop, D.*: Postgrad. Med. J., 45 (1969) 129.
3. *Chisolm, J. J. Jr.*: Sci. Am., 224 (1971) 15.
4. *Momčilović, B.*: Arh. hig. rada, 24 (1973) 131.
5. *Momčilović, B., Kostial, K.*: Environ. Res., (in print) 1974.
6. *D'Amour, F. E., Blood, F. R.*: Manual for laboratory work in mammalian physiology, Univ. Chicago Press, Chicago (1953) 3.
7. *Castellino, N., Aloj, S.*: Brit. J. industr. Med., 21 (1964) 308.
8. *Bolanowska, W., Piotrowski, J.*: Med. Pracy, 19 (1968) 133.
9. *Teisinger, J., Prerovska, I., Sedivec, V., Flek, J., Rith, Z.*: Int. Arch. Gewerbe-path. Gewerbehyg., 25 (1969) 240.
10. *Kostial, K., Simonović, I., Pišonić, M.*: Nature, 233 (1971) 564.

## ACKNOWLEDGEMENT

This work was partially supported by a research grant from the US Environmental Protection Agency and the National Institute for Occupational Safety and Health, U. S. A.

*Sažetak*USPOREDBA METABOLIZMA VIŠIH DOZA OLOVA U MLADIH  
I ODRASLIH ŠTAKORA

U štakora starih 15 i 120 dana istraživali smo kinetiku retencije i eliminacije olova nakon jednokratne parenteralne doze od 500  $\mu\text{g}$  Pb/kg tjelesne težine uz dodatak  $^{203}\text{Pb}$  (50  $\mu\text{Ci/kg}$ ). Osmog dana bio je postotak retencije radioaktivnog olova osam puta viši u mozgu, dvaput u femuru i jetri, pola puta viši u krvi i zubima, a dvaput niži u bubrezima mladih nego u odraslih štakora. Te su razlike u skladu s rezultatima našeg ranijeg rada o kinetici vrlo niskih doza olova u mladim i odraslim štakora. Povišenje doze izazvalo je u ovim pokusima viši postotak retencije i sporiju eliminaciju radioaktivnog olova iz tkiva mladih i odraslih štakora.

*Primljeno 18. IV 1974.*

*Institut za medicinska istraživanja  
i medicinu rada JAZU, Zagreb*