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*SHORT COMMUNICATION*

# Effect of Prenatal and Postnatal Exposure to Lead on Kidney Function in Male and Female Rats

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**The effect of 5 months' exposure to 0.5% lead acetate in drinking water on the kidney function of developing rats was studied. In both sexes, lead exposure produced a significant elevation of the kidney weight and after 3 months' treatment both male and female rats showed signs of tubular impairment. In male rats increased $\beta_2$-microglobulin and lactate dehydrogenase excretion was observed. Lysozyme was increased after 5 months of exposure. No changes were observed in total proteins and albumin excretion. Female rats showed a significantly increased excretion of $\beta_2$-microglobulin from 3 months onwards, while lactate dehydrogenase increased only at the end of 3 months and total proteins after 5 months of exposure. No changes were observed in lysozyme and albumin excretion. Thus, the results suggest that lead exposure produces changes in the renal tubular function of developing rat. There is no sex difference in the nephrotoxicity of lead. Comparison with our previous studies suggests that exposure to lead starting at weaning is more renotoxic than exposure starting 2 months later. However, prenatal exposure might also have been a contributory factor.**

## INTRODUCTION

Recent evidence suggests that occupational and environmental exposure to lead may contribute to a significant number of cases of chronic renal disease.[1] Thus, the consequence of environmental exposure to lead in early life may be chronic renal disease in adults exposed occupationally to this heavy metal. Prolonged administration of lead to rats ultimately results in renal lesions similar to those seen in man. Thus, an experimental animal model for chronic lead nephropathy is available.[2] The present study was designed to examine some of the functional changes that occur in kidneys of male and female rats that have been prenatally and postnatally exposed to 0.5% lead acetate. This concentration did not induce nephrotoxic effects in adult animals.[3]

## METHODS

SPF Wistar rats of 5 weeks (females) or 3–4 months (males) old were used. A control group of female rats was given demineralized water and the exposed group received drinking water with 0.5% lead acetate. After 6 weeks, females were mated with intact males. The exposure of mothers continued during gestation and lactation. Weaning (28-day-old) offspring were separated by sex and were given drinking water with the same lead concentration. After 1, 3 and 5 months of exposure, eight control and eight exposed rats of each sex were placed in individual metabolism cages to collect 24-h urine. After 3 and 5 months of exposure, rats were sacrified by decapitation. Urinary proteins and enzymes were determined by the methods described in our previous reports.[3,4] Blood lead was determined by atomic absorption spectrometry. Data were evaluated by two-way variance analysis and one-tailed *t*-test.

## RESULTS AND DISCUSSION

The presence of 0.5% lead acetate in the drinking water decreased the daily water consumption of male rats from 40.0 ± 1.1 ml (SEM) to 29.9 ± 0.9 ml and that of female rats from 30.3 ± 1.1 to 26.4 ± 1.9 ml in the first 3 months (after weaning) and from 38.0 ± 0.5 to 31.0 ± 0.5 ml (males) and from 33.0 ± 0.5 to 31.7 ± 1.0 ml (females) after 4 and 5 months. The average daily lead intakes of male and female rats in the first period were 365 ± 23 and 313 ± 15 mg $kg^{-1}$ and in the second period 268 ± 10 and 309 ± 12 mg $kg^{-1}$, respectively. At sacrifice, 3-month-old male and female rats had 179.5 ± 5.6 and 135 ± 7.6 and 5-month-old male and female rats had 222.2 ± 9.8 and 149 ± 6.0 μg lead 100 $ml^{-1}$ blood. The corresponding blood lead concentrations were 4.6 ± 0.6 and 4.5 ± 0.9 μg 100 $ml^{-1}$ in control male

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**Table 1. Effect of exposure to 0.5% lead acetate on the urinary excretion of albumin, total proteins, $\beta_2$-microglobulin, lysozyme and lactate dehydrogenase, and kidney weight in rats[a]**

| | | Albumin[c] ($\mu g\ 24\ h^{-1}$) | Proteins[b] ($mg\ 24\ h^{-1}$) | $\beta_2$-microglobulin[b] ($\mu g\ 24\ h^{-1}$) | Lactate dehydrogenase[c] ($mU\ 24\ h^{-1}$) | Lysozyme[c] ($\mu g\ 24\ h^{-1}$) | Kidney weight[c,d] ($g\ kg^{-1}$) |
|---|---|---|---|---|---|---|---|
| *Male rats* | | | | | | | |
| After 1 months' exposure | Control | 79 ± 11 | 5.0 (2.7–6.7) | 1.2 (0.2–10.2) | 123 ± 18 | 8.22 ± 1.51 | – |
| | Pb exposure | 73 ± 13 | 8.5 (5.7–12.0) | 2.2 (0.4–9.4) | 144 ± 20 | 7.12 ± 1.18 | – |
| After 3 months' exposure | Control | 115 ± 33 | 4.6 (2.2–9.5) | 6.2 (3.5–9.7) | 130 ± 22 | 8.08 ± 1.50 | 6.1 ± 0.2 |
| | Pb exposure | 121 ± 31 | 4.8 (2.0–19.8) | 13.1 (7.9–21.8)*** | 241 ± 45* | 9.48 ± 1.36 | 6.8 ± 0.3* |
| After 5 months' exposure | Control | 141 ± 32 | 4.9 (3.0–9.2) | 5.4 (2.4–20.0) | 120 ± 22 | 10.23 ± 1.99 | 5.7 ± 0.2 |
| | Pb exposure | 113 ± 20 | 4.9 (1.6–8.1) | 11.1 (5.0–16.0)** | 223 ± 56* | 18.25 ± 4.45* | 7.0 ± 0.2*** |
| F-test | Pb exposure | 1.08 | 1.65 | 7.85** | 8.48** | 2.31 | – |
| | Time | 7.65** | 2.02 | 20.28*** | 1.40 | 4.92* | – |
| *Female rats* | | | | | | | |
| After 1 months' exposure | Control | 90 ± 15 | 1.5 (0.8–2.8) | 1.2 (0.3–1.6) | 65 ± 9 | 9.59 ± 2.27 | – |
| | Pb exposure | 135 ± 18 | 1.5 (0.5–2.4) | 2.0 (1.4–3.2) | 84 ± 26 | 10.91 ± 1.59 | – |
| After 3 months' exposure | Control | 164 ± 32 | 1.3 (0.9–4.3) | 2.5 (1.5–4.4) | 80 ± 22 | 9.86 ± 1.62 | 6.2 ± 0.3 |
| | Pb exposure | 258 ± 84 | 1.6 (0.9–3.0) | 5.4 (2.1–12.1)** | 180 ± 28* | 12.28 ± 2.45 | 7.3 ± 0.3* |
| After 5 months' exposure | Control | 192 ± 35 | 1.8 (0.9–4.0) | 3.0 (1.4–6.1) | 62 ± 27 | 10.95 ± 2.31 | 6.5 ± 0.4 |
| | Pb exposure | 274 ± 51 | 3.6 (1.5–10.7)* | 5.4 (1.8–15.8)* | 83 ± 19 | 9.51 ± 1.17 | 7.2 ± 0.2* |
| F-test | Pb exposure | 3.79 | 3.58 | 14.59*** | 4.37* | 0.17 | – |
| | Time | 3.78 | 4.74* | 13.69*** | 2.73 | 0.09 | – |

[a] Data are evaluated by two-way variance analysis and Student's *t*-test; * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$.
[b] Geometric mean (range) of eight animals.
[c] Arithmetic mean ± SEM of eight animals.
[d] Kidney weights are expressed in $g\ kg^{-1}$ body weight.

rats and 2.8 ± 1.1 and 2.2 ± 0.8 $\mu g\ 100\ ml^{-1}$ in control female rats.

Table 1 shows that 3 months' treatment of male rats caused tubular impairment with increased $\beta_2$-microglobulin and lactate dehydrogenase excretion. Lysozyme was increased after 5 months of exposure. Female rats showed a significantly increased excretion of total proteins after 5 months, lactate dehydrogenase after 3 months and $\beta_2$-microglobulin after 3 and 5 months. The kidney weights of lead-treated animals of both sexes were significantly higher than those of the conrol groups after 3 and 5 months. The lack of increase in albumin excretion indicated that glomerular function was not impaired.

This study suggests that lead exposure in the developmental period may be important in determining renal toxicity. Because in our previous studies[3,4] exposure started 2 months later, either the 2-month difference in age or the exposure of the parents affected the sensitivity of kidney to lead. There is no sex difference in the nephrotoxicity of lead.

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