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Effect of Exposure to Lead on Reproduction in Male Rats

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Historically, lead is a known abortifacient and spermicidal agent in conditions of high exposure (Thomas and Brogan 1983). Decreased fertility in men occupationally exposed to moderate lead levels has been documented via spermatic alterations (Lancranjan et al. 1975; Wildt et al. 1983). Several animal studies confirm adverse reproductive action of lead administration in males but many of them reported no apparent effect (Zirkin et al. 1985; EPA 1986). Available results do not provide definite information on exposure levels at which specific toxic effect of lead on male reproduction might occur. Because of the paucity of human data more animal data are needed to clarify this aspect of lead toxicity.

The objective of present study was to determine the effect of chronic oral exposure to different levels of lead on male reproductive performance since oral exposure data are more relevant to human environmental exposure. Additionally, most previous results have been obtained after parenteral administration of lead. Our experiments were performed on rats by using the incidence of pregnancy to assess male fertility and litter size and pup weight as indicators of the lead effect on perinatal development. Similar parameters were used in reproduction studies by other authors (e.g. Stowe and Goyer 1971).

MATERIALS AND METHODS

The experiments were performed on sexually mature albino rats of both sexes from the Institute's breeding farm. Male rats had an initial mean body weight of about 250 g. The exposed males were administered lead acetate (p.a. "Kemika", Zagreb) in distilled water as beverage for 18 weeks. They were grouped according to

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three levels of exposure: 1500, 3500 and 5500 ppm of lead (or approximately 155, 350 and 550 mg/kg/day). The control males as well as female rats received distilled water. Throughout the experiments all animals were housed in macralon cages (10 animals in each) provided with stainless steel bottoms and lids, with free access to beverage and standard rat food ("Sljeme", Zagreb).

The control and the exposed males were bred twice with unexposed females: four and thirteen weeks after the beginning of exposure to lead (two females with one male). In this way the first offspring (F_{1a}) was obtained after shorter and the second (F_{1b}) after longer exposure of the fathers.

Fertility of male rats was assessed by the incidence of pregnancy (%) in females they had been mated with. Other reproductive parameters determined were number per litter and mean body weight (g) of newborn and 11-day-old pups. Health indicators recorded in adult males were: general appearance, mortality rate (%), body weight (g) and average daily food (g) and beverage (ml) consumption.

RESULTS AND DISCUSSION

Exposure to three different levels of lead in drinking water produced no overt signs of general toxicity in adult male rats. Only at the end of the exposure period (18 weeks) the mean body weight of males exposed to two higher lead levels, i.e. 3500 and 5500 ppm, was slightly lower (97 and 96% of control values respectively). In the group exposed to 1500 ppm of lead it did not differ from the controls. The average daily food consumption in exposed males was the same as in controls: 20 to 25 g/day. The average beverage consumption in the three exposed groups was reduced by about 10, 25 and 28% respectively compared to normal water intake in controls of about 40 ml/day. Mortality rate of male rats did not exceed 2% in any of the four observed groups throughout the experiment.

There was no effect of lead exposure on male fertility either after the first (shorter exposure) or after the second mating (longer exposure to lead). It should be mentioned that in rat the time required for proliferating spermatogonia to develop into mature spermatozoa is 51.6 days and that one of the four seminiferous epithelial cycles lasts 12.9 days (Desjardins 1985). Thus in our experiments shorter 4-week premating exposure to lead had covered 2 cycles of seminiferous epithelium. Longer 13-week premating exposure of males was

of sufficient duration to affect more than one entire process of spermatogenesis if any. After both matings the pregnancy incidence values in mated females were within the range of controls (60 to 70%). Table shows the values of the average number per litter of live newborn and 11-day-old rats, as well as their body weights (g) in the first (F_{1a}) and in the second (F_{1b}) offspring. It can be seen that values in the three exposed groups of pups did not differ from controls in both groups of offspring.

There is increasing evidence in literature that reproductive performance in males can be affected by exposure to toxic agents (EPA 1986). Adverse effects of lead on their offspring include decreased litter size, birth weight and survival (Stowe and Goyer, 1971; Ivanova-Chemishanska et al. 1980). However, few studies have reported no apparent effect of lead on aspects of male reproduction (Azar et al. 1973; Zirkin et al.1985). The lack of consistency in available experimental data dealing with reproductive effect of lead in males has resulted from the facts that only few studies have examined the dose-response effects and also that lead had been administered in various forms, doses and routes, as well as to different animal species.

According to our previous findings reproductive effects of lead observed in progeny born to the exposed mothers were marginal when the females had been exposed to 3500 ppm lead in drinking water (Piasek and Kostial 1984). After longer exposure to 5500 ppm lead in beverage the adverse effects on female reproductive performance were significant (Piasek and Kostial 1985). In the present experiments lead (acetate) was administered in the same way (form, doses, route and length of exposure) to adult male rats as in our previous experiments on females. All three levels of lead exposure (1500, 3500 and 5500 ppm) produced no adverse effect on male fertility. There was also no effect on number and/or body weight of their offspring born either after shorter or after longer exposure period. These levels of lead caused no deleterious health effect in exposed females (Piasek and Kostial 1985), nor in exposed male rats.

It might be concluded that in identical exposure conditions, in which adverse effect of lead on female reproductive performance had been obtained, no paternally mediated reproductive effect in rats was observed.

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Table. Influence of male rat exposure to increasing doses of lead (1500, 3500 and 5500 ppm) in drinking water on average number per litter and mean body weight of newborn and 11-day-old pups in the first and second offspring

Groups (mating combinations)	No. of live pups/litter		Weight of pups (g)	
	Days after birth			
	0	11	0	11
C ♀ C ♂	[a]8.4±0.4 (53)	5.9±0.6 (50)	5.1±0.1 (50)	15.1±0.5 (38)
	[b]8.3±0.3 (76)	7.4±0.4 (73)	5.5±0.1 (73)	18.4±0.4 (67)
C ♀ E ♂$_{1500}$	8.1±0.5 (25)	6.8±0.7 (24)	5.5±0.1 (24)	17.3±0.7 (21)
	8.8±0.7 (20)	7.7±0.8 (19)	5.3±0.1 (19)	16.2±0.8 (17)
C ♀ E ♂$_{3500}$	8.1±0.8 (21)	6.3±1.0 (18)	5.2±0.1 (18)	15.5±0.6 (13)
	7.1±1.0 (17)	6.2±1.1 (14)	5.6±0.2 (14)	17.7±1.3 (12)
C ♀ E ♂$_{5500}$	9.9±0.6 (31)	8.9±0.6 (29)	5.2±0.1 (29)	15.9±0.6 (27)
	8.2±0.9 (21)	8.7±0.8 (19)	5.6±0.1 (19)	18.3±0.7 (19)

Results are presented as arithmetic means ± SEM (number of litters in parentheses).

C - control, E - exposed - lead in ppm: 1500, 3500 and 5500.

[a]First offspring (F_{1a}) - 4-week premating exposure of fathers

[b]Second offspring (F_{1b}) - 13-week premating exposure of fathers

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