Bull. Environm. Contam. Toxicol 26, 647-651 (1981)

Splenomegaly and Adrenal Weight Changes in Isolated Adult Mice Chronically Exposed to Lead

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Inorganic lead is an environmental contaminant of continuing toxicological concern. Since the effects of chronic lead ingestion are most pronounced in neonatal or very young animals, investigations relating to the mental health effects of lead on children have to date been of prime importance (BRYCE-SMITH et al. 1978). As the perspective of lead toxicity has widened, however, concern about the effects of lead exposure in adults has also been expressed (GRANDJEAN 1978), and several studies have now documented lead-induced learning abnormalities in adult animals (OGILVIE 1977, LANTHORN & ISAACSON 1978, CORY-SLECHTA & THOMPSON 1979).

Recently we have shown that lead-treated adult mice fail to develop the isolation-induced aggressiveness typical of untreated control animals (OGILVIE & MARTIN 1980). Animal aggression has both neural and endocrine substrates (MOYER 1976), and with regard to the latter, it is well known that many mammals exhibit changes of adrenal weight and function when subjected to irritable aggression associated with the pressure of population density (VAUGHAN 1972).

Although impairment of adrenal gland functioning has been reported for lead-poisoned humans (DAMSTRA 1977), few animal studies have yet investigated the effects of chronic lead exposure on the pituitary-adrenal axis. In this paper we describe changes in adrenal weights for mice subjected to isolation and lead exposure. In addition, since it is well known that lead exposure can reduce the survival time of red blood cells (HERNBERG et al. 1967), we also investigated the possibility that the spleen, the disposal center for discarded red cells, might also be affected by lead exposure.

METHODS

Two weight-matched groups of male, 25 to 34 g Swiss-Webster mice were individually housed in 13x29x12 cm cages at 22 $\pm$ 1 ^{o}C, under a 12L:12D photoperiod. Rat chow and water were freely available. Lead-treated

0007-4861/81/0026-0647 $01.00

animals were given distilled water containing 5 mg/ml of lead acetate (2732 μg Pb/ml), while control mice drank tap water. At intervals of 2, 4 and 6 weeks, a final body weight was obtained, and then 5 control and 5 lead-treated mice were given an overdose of nembutal. Adrenal glands and spleens were excised, trimmed of extraneous tissue and weighed. In addition, spleen weights were also determined for a small group of mice from a related experiment. These animals had ingested a 5 mg/ml lead acetate solution during 5 to 10 months of isolation.

RESULTS

The lead treatment used in this study produced no mortality and no inhibition of weight gain. After 2 weeks of isolation and lead treatment, the mean adrenal weights for the control and lead-treated mice were approximately equal (Fig. 1), however, after 4 and 6 weeks the control mice had smaller adrenals. This difference was significant at 4 weeks ($t = 3.02$, $P < 0.025$), but not at 6 weeks. Analysis of the changes in adrenal weights with increasing time of isolation (by one-way ANOVA) revealed that the decrease is significant for the control mice ($F = 7.30$, $F_{0.01} = 6.93$, $P < 0.01$), but not for the lead-treated animals ($F = 3.59$, $F_{0.05} = 3.88$).

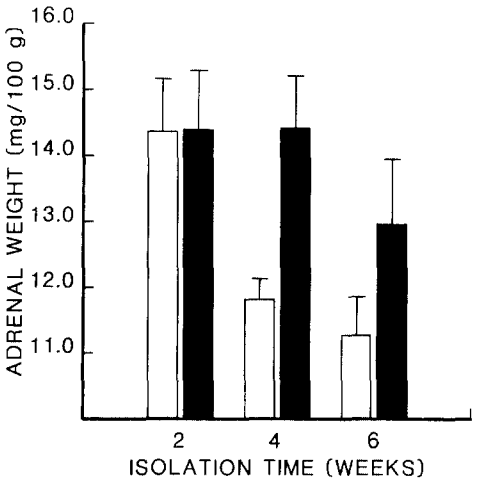

FIG. 1. Mean adrenal weights for isolated control mice given tap water (open bars), and mice given a drinking solution containing 5 mg/ml of lead acetate (black bars). The data are represented as the mean + 1 standard error for 5 animals.

The effect of lead treatment on the spleen weights of isolated mice is summarized below in Table 1. In every case, the lead-treated mice on average had larger spleens than their respective controls. Analysis of the change in spleen weights with time by one-way ANOVA indicated that the increase in spleen weight evident for lead-treated mice is highly significant ($F = 7.38$, $F_{0.01} = 5.42$, $P < 0.01$). However, spleen weights for control mice did not change significantly during the period of isolation ($F = 0.27$).

Spleens from mice that had been exposed to lead for 6 weeks were 29% heavier than spleens from control mice, while for mice that had ingested 5 mg/ml of lead acetate for 5 to 10 months, the increase in spleen weight was more than 130% over untreated controls. The degree of splenomegaly resulting from this relatively long exposure to lead is evident in Fig. 2, in which spleens from 2 mice exposed to lead for 10 months are shown.

TABLE 1

Effect of lead acetate (5 mg/ml in the drinking water) on the spleen weight of isolated albino mice

Exposure time	Spleen weight (% of body weight) Control	Lead-treated	% increase
2 weeks	0.234 ± 0.026(5)*	0.260 ± 0.011(5)	11.1
4 "	0.261 ± 0.019(5)	0.264 ± 0.018(5)	1.2
6 "	0.261 ± 0.020(5)	0.336 ± 0.020(5)	28.7
5 to 10 mo.	0.240 ± 0.047(4)	0.573 ± 0.055(4)	138.8

*The data are given as the mean ± 1 standard error for the number of animals in brackets.

DISCUSSION

The significant fall in control adrenal weights following isolation (Fig. 1) is in agreement with previous reports that isolated mice have smaller adrenals than group-housed animals (BRAIN 1972, BENTON et al. 1978). With respect to the lead-treated mice, it appears that the lead exposure delayed the anticipated decline in adrenal weight. This explanation seems compatible with one of the few previous reports dealing with the effects of lead on the adrenal gland. In this study, rats fed a diet containing 1% lead acetate exhibited a transitory enlargement of the adrenals (WRIGHT et al. 1975).

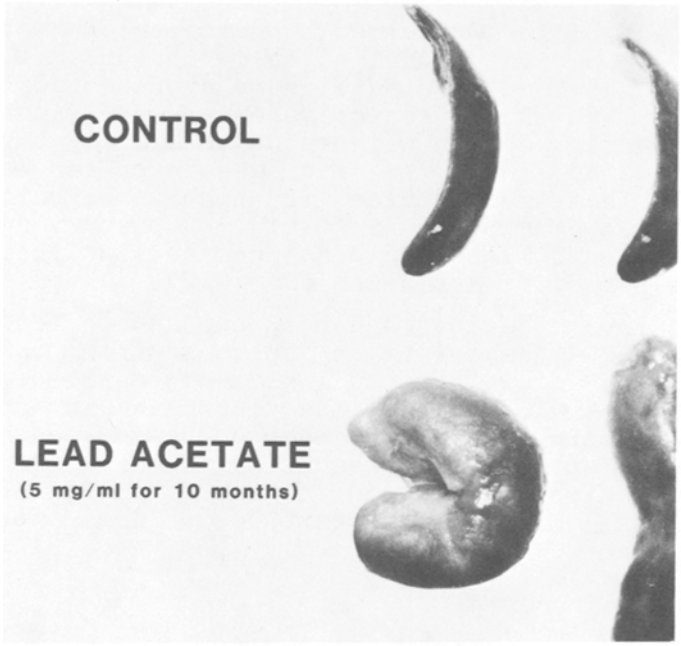

FIG. 2. Spleens removed from albino mice that had been isolated for 10 months. During this time the animals drank either tap water (controls), or a 5 mg/ml solution of lead acetate.

In a recent study (OGILVIE & MARTIN 1981) that involved the same conditions of isolation and lead treatment used in the present series of experiments, we confirmed earlier reports of increased aggression in isolated mice (VALZELLI 1973, BRAIN 1975). In addition, we observed that such aggressiveness failed to develop in mice subjected to lead treatment during the isolation period. Since it is known that subordinate animals have heavier adrenals than dominants (BRAIN 1972, McKINNEY & PASLEY 1973), the observation in the present study of heavier adrenals in isolated lead-treated mice suggests that lead-induced adrenal weight changes may be associated with the failure of lead-treated mice to develop isolation-induced aggressiveness.

Lead exposure can reduce the survival time of red blood cells (HERNBERG 1967). In addition, the spleen sequesters damaged cells and increases in size in proportion to the demand for red cell disposal (RIFKIND 1966). These facts may account for the observed increase in spleen weight with increasing time of lead exposure. Lead-induced splenomegaly has been described previously. Rats fed a lead-contaminated diet

for 3 months exhibited a 216% increase in spleen weight, however, this treatment caused a significant inhibition of weight gain, and the study was further complicated by a vitamin E deficiency (LEVANDER et al. 1975). In a more recent rat study, a blood lead level of 104 µg/100 ml was associated with an increase in spleen weight of 15% (GELMAN et al. 1978). Blood lead levels were not measured for the mice used in the present study, however, we have previously determined that under conditions similar to the present study, isolated mice ingesting a 5 mg/ml solution of lead acetate had blood lead levels of 160, 101 and 522 µg/100 ml after 2, 4 and 6 weeks of treatment, while mice subjected to exposures of several months duration had blood lead levels in excess of 1000 µg/100 ml. Thus, the greater effect on spleen weight in the present study compared with the much smaller change described above for rats, probably reflects differences in blood lead levels, as well as possible species differences in lead sensitivity.

Acknowledgement. This study was supported by an Operating Grant from the Medical Research Council of Canada.

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