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# Blood Lead Concentrate and Blood Pressure after $CCl_4$ Treatment

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There have been inconsistent reports of the association between lead (Pb) and hypertension in rats. Two groups of investigators failed to affect hypertension in rats (Padilla et al 1969, Pardoc 1952), while two other groups (Griffith and Lindauer 1944, Diaz-Rivera and Horn 1945) reported that Pb did produce hypertension. In a recent report (Victery et al 1982) it was concluded that doses of Pb that cause Pb concentrations typically found in the general population are capable of bringing about moderate hypertension in the rat.

Renal hypertension has been reduced to normal blood pressure levels with carbon tetrachloride ($CCl_4$) treatment in the rat (Loyke et al 1960, Loyke 1964). Cross perfusion of chronic Grollman renal hypertension with normotensive $CCl_4$ treated rats resulted in blood pressure reduction, suggesting that a vasodepressor substance was present in the $CCl_4$ treated animals (Loyke and Hoobler 1982). Since Pb has been found to influence blood pressure in rats (Diaz-Rivera and Horn 1945), the pressure and Pb levels were measured in renal hypertensive, spontaneous hypertensive rats (SHR), normotensive, and $CCl_4$ treated and untreated rats to determine whether blood Pb levels are altered in an attempt to characterize the vasodepressor substance and relate those levels to blood pressure.

## METHODS AND MATERIALS

Twenty-one male Sprague-Dawley rats approximately nine weeks old were obtained from Beaumanor Farms and twelve spontaneous hypertensive rats (SHR) from The Taconic Farms. All animals weighed approximately 200 g. and were housed in individual cages and given Purina chow, free of Pb. Tap water with a Pb level of $<1\mu$/dl was given ad lib. All animals were weighed weekly and blood pressure measured by the tail cuff method (Friedman and Freed 1949). Nine animals were made renal hypertensive by the Grollman method (Grollman 1944) ligating both poles of one kidney with contralateral nephrectomy one week later. Of the 21 animals, 7 normotensive were given 0.15 ml of analytical grade $CCl_4$ subcutaneously two times a week for a total of 20 doses; along with 3 renal hyper-

tensive animals. Five normotensive and 6 renal hypertensive animals were untreated as controls. Of the 13 SHR animals, 5 were treated with $CCl_4$ and the remaining 7 were untreated. Tail blood samples for Pb measurement, erythrocyte counts, and hemoglobin levels were obtained one day after the last dose period of $CCl_4$ in the normotensive and SHR groups. Lead concentrations were determined in triplicate directly from a Varian Model AA-475 Atomic Absorption Spectrophotometer using a graphite furnace (Behari 1981). The Student's "t" test was used for computing the significance between the hypertensive and normotensive animals and the $CCl_4$ treated hypertensive and control animals.

## RESULTS AND DISCUSSION

A statistically significant decrease in blood pressure ($P<.001$) was manifest in the chronic renal hypertensive animals treated with $CCl_4$ in relation to their untreated control animals (Table 1). Likewise the SHR animals treated with $CCl_4$ had a statistically significant decrease in blood pressure ($P<.001$). In contrast the blood pressure of the normotensive treated animals were similar compared to their untreated controls (Table 1).

Lead levels were decreased ($P<.001$) in both the normotensive and renal hypertensive animals treated with $CCl_4$ (Table 1) in relation to their untreated control animals. The SHR lead values were lower than that found in the renal hypertensive and normotensive animals (Table 1). Treatment with $CCl_4$ also lowered the lead levels in the SHR animals but not to a statistically significant degree.

No essential change was found in the number of erythrocytes after $CCl_4$ treatment in the normotensive or the renal hypertensive animals (Table 1) and erythrocytes were counted only in the untreated renal animals.

Hemoglobin values were unchanged after $CCl_4$ treatment in the normotensive animals (Table 1) but were decreased in the SHR animals (P-NS). The untreated renal hypertensive animals had hemoglobin values similar to the SHR and the normotensive animals.

The initial mean weight for the $CCl_4$ treated group was 200 g SD ± 7.6, and their untreated controls weighed 218 g SD ± 6.0. At the end of the experiment, which lasted 4 months, the normotensive $CCl_4$ group weighed 264 g SD ± 10.5 and the untreated normotensive weighed 263 g SD ± 7.5. The untreated renal hypertensive rats weighed 242 g SD ± 7.5 and the treated ones 196 g SD ± 10.3 (sacrificed 3 weeks earlier). Final weight of the $CCl_4$ treated SHR animals was 248 g SD ± 8.4 and 243 g SD ± 8.2 for the untreated. Renal hypertensive blood studies were measured only in the untreated animals which had mean erythrocyte count of $7.76 \times 10^{-4}$ with a hemoglobin level of $15.8 \times 10^{-4}$ (Table 1).

Table 1

Serum Lead, Blood Pressure, Weight and Hematology Values

| | NT | | SHR | | RENAL | |
|---|---|---|---|---|---|---|
| | $CCl_4$ | Untreated | $CCl_4$ | Untreated | $CCl_4$ | Untreated |
| Blood Pressure mm Hg. | 136 ± 9.8 | 132 ± 2.7 | 150 ± 5.1 | 175 ± 4.4 | 159 ± 8.1 | 195 ± 12.0 |
| Lead $\mu$g/dl | 4.63 ± 1.45 | 8.48 ± 2.79 | 2.0 ± 0.1 | 3.0 ± 1.5 | 5.4 ± 0.26 | 7.9 ± 0.86 |
| Erythrocytes $X10^{-4}$ | 9.87 ± 0.77 | 8.70 ± 0.81 | 8.18 ± 0.91 | 8.77 ± 0.82 | | 7.76 ± 1.7 |
| Hemoglobin grams | 16.7 ± 1.9 | 16.2 ± 1.0 | 13.6 ± 1.9 | 15.9 ± 1.2 | | 15.8 ± 3.3 |

The aims of this study were to examine the effect of $CCl_4$ treatment on blood Pb levels and relate blood pressure Pb levels. The amount of Pb in the rat has been found to influence blood pressure (Pardoc 1952, Fowler et al 1980), and an elevated level of Pb can cause hypertension (Pradoc 1952, Diaz-Rivera and Horn 1945). In this experiment, the level of Pb in the blood was similar in both normotensive and renal hypertensive animals. Lower Pb levels were found in the SHR animals possibly because of housing in their early life at another laboratory. Victery et al 1982 found that a blood Pb level of over 18.2 µg/dl was needed to produce hypertension in the rat which is considerably higher than the level found in our Grollman renal hypertensive animals (8.06 µg/dl). Since our normotensive blood Pb level was similar to the renal hypertensive group, it may be concluded that Grollman renal hypertension is not caused by elevated Pb levels. Untreated rat Pb blood levels (Fowler et al 1980) were found to be between 5-23 µg/dl which was within the range of our controls.

Treatment with chronic subcutaneous doses of $CCl_4$ to normotensive rats significantly lowered blood Pb levels. Whether lower than normal blood levels of Pb are an advantage for the rat in controlling blood pressure is questionable, since Perry et al (1979) found that extremely low levels of Pb (1ppm) added to the diet can cause hypertension while Victery et al (1982) reported that extremely high levels (500 ppm) were unable to produce hypertension. This study did not add Pb to the diet.

Fowler et al (1980) reported blood Pb levels in normotensive untreated rats which were similar to our Pb values but no references were found for Pb values in hypertensive animals. Treatment with $CCl_4$ to chronic Grollman renal hypertensive rats resulted in blood pressure reduction as seen before (Loyke et al 1960, Loyke 1964) with a significant reduction in blood Pb levels as was observed in normotensive animals. Spontaneous hypertensive rats likewise had a reduction in blood pressure and Pb levels after $CCl_4$ treatment. These studies demonstrate that $CCl_4$ treatment lowers both blood pressure and blood levels of Pb in the rat.

Mahaffrey and Goyer (1972) found that the presence of iron deficiency anemia in $CCl_4$ treated animals resulted in enhancement of Pb retention by increasing Pb retention in kidney, liver and bone. There was no evidence of an iron deficiency anemia in these normotensive $CCl_4$ treated rats, and Fowler et al (1980) reported that a hemopoietic system may not be a sensitive indicator of longterm Pb contact. The data collected does not permit the distinction between a reduction in whole body Pb and a selective decrease in erythrocyte Pb content. The erythrocyte counts were not decreased in the normotensive $CCl_4$ treated animals which suggests that the decrease in Pb was outside of the erythrocyte since most of the Pb

resides in the erythrocyte.

Numerous studies relating to Pb and blood pressure involve the addition of Pb to animal diets (Diaz-Rivera and Horn 1945, Perry et al 1979). No Pb was added to the rat's diet in this study and the only source of Pb would be that found in drinking water and city air. Urban dust contains Pb in concentrations between 1000 and 5000 mg/g and urban air between 2 and 5 mg per cubic meter (Needleman 1977). Analysis of our drinking water had less than 1 ppm of Pb.

While $CCl_4$ treatment did not affect blood pressure in normotensive rats, the blood Pb content was significantly reduced. Treatment with $CCl_4$ did reduce blood pressure in chronic Grollman hypertensive animals and was accompanied by a lower level of Pb in the blood than that found in the normotensive or hypertensive untreated groups. The $CCl_4$ treatment and/or the vasodepressor substance, previously demonstrated, may be affecting Pb metabolism in the rat.

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