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Effect of Chronic Lead Intoxication on *in vivo* I^{131} Uptake By the Rat Thyroid.* (31656)

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Lead poisoning continues to be an important industrial hazard, and in recent years has become a problem affecting persons who consume illicit whiskey(1). We have found impaired I^{131} uptakes responsive to TSH in patients with plumbism and have suggested that this abnormality is caused by the metal (2). Porritt(3) previously had suggested an impairment of thyroid function by lead in 1931, and Kremer and Martin(4) reported a case of coexisting myxedema and plumbism in 1955.

To test this hypothesis, rats were chronically intoxicated with lead and *in vivo* radioactive iodine uptakes measured. The findings are the subject of this report.

Methods. Male and female weanling Sprague-Dawley rats were placed in cages, 3 of a sex to a cage, and fed Purina laboratory chow. Tap water was given the control animals; lead acetate dissolved in tap water in concentrations of 1 g/liter and 4 g/liter was given the experimental group. After 6 months all animals were fed a Remington low-iodine diet for 2 months and 24-hour *in vivo* I^{131} uptakes were determined. The uptakes of 6 female and 3 male controls were essentially the same as 7 females and 6 males receiving 4 g of lead acetate/liter of drinking water. The concentration of lead acetate was then increased to 8 and 12 g/liter of water. These concentrations of lead (1, 4, 8, 12 g/liter) were given because previous studies had shown that two effects of lead intoxication, anemia and renal tubular inclusions, occur in the rat at this dose level, without death of the animal. Thyroid studies were repeated after 2 to 6 months of feeding Purina laboratory chow plus the increased ingestion of lead. The low-iodine diet was fed for 2 weeks and the *in vivo* thyroid I^{131} uptake determined at 1, 2, 3, 6, 12, and 24 hours. The uptake curve was determined because previous measurement of the uptake at 24 hours had shown little difference between the experimental and control animals. The rats were killed at the end of the expirement and the conversion ratio, *in vitro* I^{131} uptake, thyroid weight, and hematocrits were measured. Urinary and fecal excretion of I^{131} was not measured.

In vivo I^{131} uptake was determined using light nembutal anesthesia and subcutaneous administration of sufficient I^{131} to give epithyroid counts at 1 hour of at least 9 to 10 times background. The rats were tied to a wooden stand over which a 1/2 inch thick lead shield, having a 1/4 inch diameter hole, was placed. The shield was flush with ventral surface of the rat with the hole directly over the thyroid. A wide field columator with sodium iodide crystal was placed directly above the hole in the shield. Emissions were counted using a Nuclear of Chicago model 132B coun-

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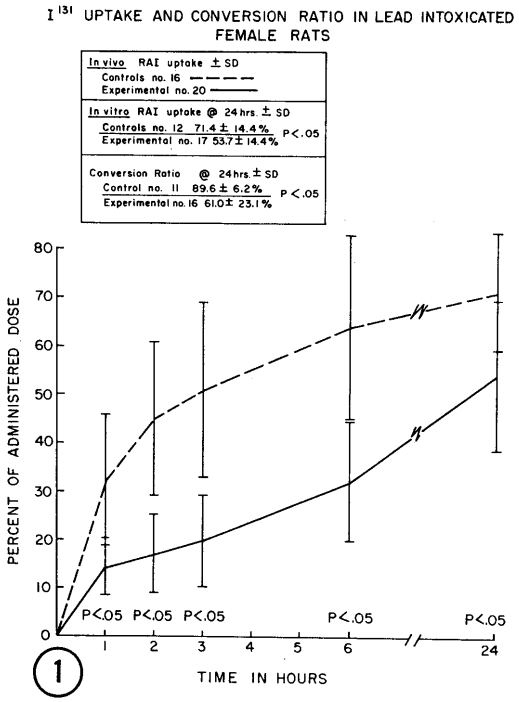

FIG. 1.

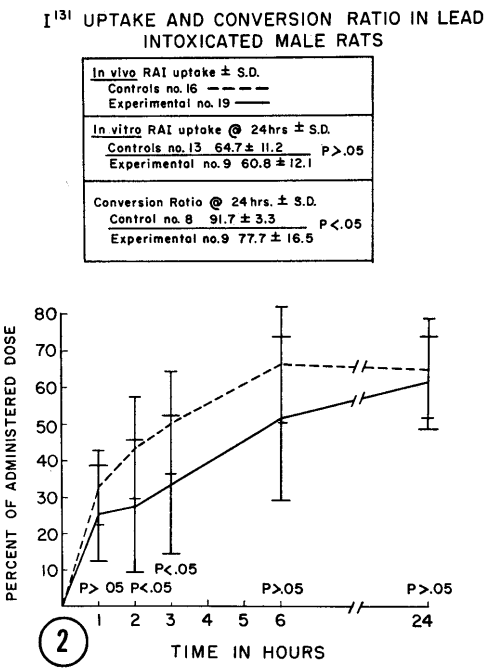

FIG. 2.

ter. A standard of volume approximately equal to the size of a rat thyroid was placed in a small polyethylene tube which was plugged at one end with paraffin and collodion at the other. The standard was placed upright in modeling clay below the hole in the shield in a position similar to the rat thyroid.

In vitro I^{131} uptakes were measured at 24 hours using a well counter. Conversion ratios were determined on heart blood according to the ultrafiltration technique of Prasad *et al*(5). Counts of the plasma were 20 to 40 times background. Counts in the ultrafiltrate were at least 10 times background. Organification of I^{131} was evaluated by the thiocyanate test(6). Thyroids were weighed prior to *in vitro* counting and hematocrits were determined on heart blood.

Results. Fig. 1 shows the findings in 16 control and 20 experimental female rats. Lead intoxication resulted in a significant decrease in I^{131} uptake, conversion ratio, and *in vitro* 24-hour I^{131} uptake. *In vitro* uptakes were similar to the *in vivo* 24-hour values in each animal, confirming the reliability of the *in vivo* technique. Fig. 2 shows the findings in the male rats. Separation between intoxicated and control groups was less than among the females. Although the average values for I^{131} uptake were lower in the intoxicated males, statistically significant differences were found only at 2 and 3 hours. *In vitro* 24-hour uptakes were not significantly different. Conversion ratios were significantly decreased in 9 experimental males compared to 8 controls. The apparent sex difference in susceptibility to lead intoxication, as far as thyroid function is concerned, may be seen by comparing the two Figures. Thiocyanate tests did not demonstrate a lesion in organification of I^{131} in the intoxicated animals.

The affects of lead were similar in rats receiving either 8 or 12 g of lead acetate/liter of water. Microhematocrits were universally low in the lead-intoxicated animals (males and females) demonstrating that sufficient lead had been fed to adversely affect the hematopoietic system. The mean weight of the intoxicated male rats was 50 g less than the controls. The mean weight of the intoxicated female rats was 30 g less than the controls. The animals were not pair-fed, however, and there was

considerable overlap between the groups. Thyroid weights of intoxicated males were similar to the controls; the same was true of the females.

Discussion. These findings show that lead intoxication can impair the uptake of I^{131} by the thyroid gland *in vivo* and are in agreement with Slingerland's(7) *in vitro* demonstration that lead salts impair the uptake of iodine by thyroid slices. Studies in the human(2) have shown that the decreased I^{131} uptake can be increased in some individuals by administration of thyroid-stimulating hormone (TSH). In addition, pituitary TSH reserve has been found to be decreased. These findings suggest that the abnormalities are secondary to toxic effects of lead on the metabolic processes of cells, both at the pituitary and thyroid level. Studies of the effect of lead on sulfhydryl enzymes in the Krebs cycle are compatible with this idea. Lead apparently combines with sulfhydryl groups, thus inhibiting the enzymes(8). In addition to blocking sulfhydryl enzymes, lead may also displace iodine from a protein sulfenyl iodide carrier proposed by Cunningham(9). This would effectively inhibit the uptake of iodine by the gland and impair the iodination of thyrogloblin.

Summary. *In vivo* depression of I^{131} uptake by the rat thyroid, and the conversion ratio has been produced by chronic lead intoxication. Female rats are more susceptible than male rats.

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Renal Excretion of Some Isomeric Hexoses in the Dog.* (31657)

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It is well known that D-glucose and D-galactose are actively reabsorbed by the renal tubules and that this reabsorption can be blocked by phloridzin(1). The renal excretion of other hexoses, especially the L-isomers, has not been studied. The literature reveals that L-glucose and L-galactose may behave quite differently from the D-isomers of these hexoses. The L-forms were not transported across the intestinal mucosa(2,3) and moved across the membranes of human erythrocytes by a process of simple diffusion (4).

The glucose analogue, 3-O-methylglucose (3MG), has been found to be actively absorbed from the intestinal lumen by the same mechanism as D-glucose(3). The behavior of this compound with respect to renal excretion has not been studied. It is the purpose of this investigation to study the renal excretion of some hexose isomers in an effort to determine: 1) if the renal tubules treat these compounds in the same manner as D-glucose; 2) and if processes other than filtration are involved in the excretion of these compounds.

Experimental. Technique. I. The close arterial injection technique of Chinard(5) was

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