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Effects of Thorium on Blood and Liver Enzymes of White Rats.

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In a previous communication[1] some of the effects of thorium, zirconium, titanium and cerium on enzyme action *in vitro* were reported. Due to the peculiar physico-chemical properties of these metals, especially in respect to their precipitability in protein solutions it was deemed advisable to determine whether these effects could be observed *in vivo*. Roussy, Oberling and Guerin[2] have reported that thorium dioxide is carcinogenic when administered intraperitoneally to rats. In this investigation an attempt is being made to determine the effects produced by the intraperitoneal injection of varying amounts of soluble thorium nitrate, $Th(NO_3)_4$, on a variety of the blood and liver enzymes of the adult white rat.

The effects upon the following enzymes were investigated: blood amylase, blood lipase, blood esterase and blood phosphatase. The following liver enzymes were investigated: liver amylase, liver lipase, liver esterase, liver phosphatase, liver xanthine dehydrogenase, liver glucose dehydrogenase, and liver lactic dehydrogenase. Amylase was determined by the Willstatter-Schudel method,[3] lipase and esterase by the method suggested by Sure *et al.*,[4] phosphatase by the method described by Bodansky[5] and the inorganic phosphorus determined by the method of Fiske and Subbarrow.[6] The dehydrogenase activities were estimated by the Thunberg technique as adapted by Collett.[7]

Twenty-one adult white rats were used for the study. Two sets of controls were run. One set of controls was inoculated with physiological saline and the other received an injection of dilute hydrochloric acid equivalent to the acid strength of the thorium injected into the experimental animals. All of the animals survived

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1 Gould, B. S., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 381.

2 Roussy, G., Oberling, C., and Guerin, M., *Bull. Acad. Med.*, 1934, **112**, 809.

3 Willstatter, R., *Unters. uber Enz.*, Berlin, 1928, **1**, **2**.

4 Sure, B., Kik, M. C., and Buchanan, K. S., *J. Biol. Chem.*, 1935, **108**, 27.

5 Bodansky, A., *J. Biol. Chem.*, 1933, **101**, 93.

6 Fiske, C. H., and Subbarrow, Y., *J. Biol. Chem.*, 1925, **66**, 387.

7 Collett, M. E., *J. Biol. Chem.*, 1928, **78**, 685.

the injections of either thorium or acid although there was some sloughing at the point of inoculation when large doses of thorium or acid were introduced. The thorium-treated animals were divided into 2 groups, one receiving relatively small doses over a period of 7 days while the other received very large doses over a 5-day period. The total amount of thorium nitrate inoculated into the first group was 71.1 mg. and into the second group, 104.5 mg. The animals were killed by decapitation, the blood was collected and the serum removed for analysis. The liver was removed, washed, weighed and minced, then ground to a very homogeneous suspension. The animals were killed 1, 2, 4, 5, and 24 hours after the last inoculation.

From an analysis of the preliminary results obtained there seems to be no indication that the inoculation of thorium exerts any significant influence on the enzymic activity of the blood or liver of white rats. The results reported on the effects of thorium on phosphatase and amylase activity *in vitro* could not be observed *in vivo*.

The liver dehydrogenases show no detectable differences whether thorium or acid is introduced. Similarly, neither blood nor liver phosphatases show any variation on the thorium-treated or acid-treated animals.

Blood esterase is decreased by the injection of either thorium nitrate or acid. Similarly the liver esterase decreases after thorium or acid treatment. The variations in each case are comparable indicating that the differences are due not to the action of the metal but rather to the acid nature of the salt.

Blood and liver lipase were also slightly decreased on the injection of either thorium or the equivalent of acid. The effect was inappreciable one hour after inoculation and undetectable after 24 hours. After 3 hours there was an apparent but small decrease.

Liver amylase was unaffected by either thorium or acid. Blood amylase showed a small decrease in activity 2 hours after inoculation of either acid or thorium. After 4 hours there was still decreased activity but after 5 hours the amylase reached the normal level.

It appears that thorium nitrate in the quantities used exerts no effects upon certain blood and liver enzymes other than would be produced by the equivalent amount of acid.