Sensitization by Thallium to Dihydrotachysterol Overdosage.* (26354)

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Chronic intoxication with thallium salts produces loss of hair occasionally accompanied by convulsions, skeletal deformities, and clouding of the lens reminiscent of tetanic cataracts. This syndrome has been compared to hypoparathyroidism and was thought to result from some primary damage to the endocrine system(1). However, the voluminous literature on thallium intoxication is rather contradictory, because of the great variability in results obtained by different investigators(2,3).

Recently, we found that highly selective calcification in the cortico-medullary junction line of the kidney is consistently obtained in rats given a single dose of thallium acetate and of dihydrotachysterol (DHT), even though, in the amount administered, neither substance in itself causes nephrocalcinosis. The thallium acetate also accentuates other manifestations of DHT-intoxication, so that a synergism between this vitamin-D derivative and thallium can readily be demonstrated.

Methods. Forty female Sprague-Dawley rats, with an average initial body weight of 95 g (range: 90-102 g), were subdivided into 4 equal groups and treated as indicated in Table I. Thallium acetate, 2 mg in 0.2 ml of water and DHT ("Calcamin," Wander), 500 μg in 0.5 ml of corn oil, were administered subcutaneously and by gavage, respectively, once on the first day. For control purposes, one group of rats was restrained with adhesive tape, in the prone position, during the 24 hours immediately following DHT-administration, to verify that the thallium salt did not act merely by virtue of its stressor effect.

Earlier observations had shown that the trauma of epilation precipitates cutaneous calcinosis in the DHT-sensitized rat(4). To determine whether this action of DHT is likewise aggravated by concurrent treatment with thallium, the hair was removed by plucking over the calvarium in all 4 groups on the second day.

The experiment was terminated on the 8th day and degree of calcification in skin, kidney, aorta, and heart was appraised by loupe-inspection in terms of an arbitrary scale: 0 (no lesion), 1 (just detectable lesion), 2 (moderate lesion), and 3 (maximal lesion). The data were subsequently checked by v. Kóssa's silver nitrate technic on histologic

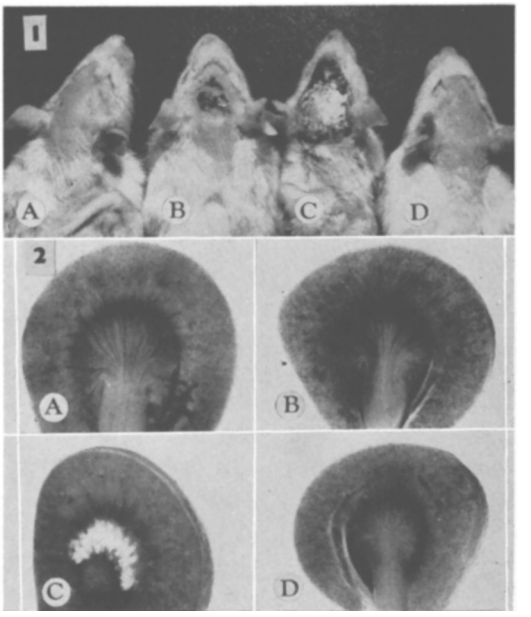

FIG. 1. Appearance of epilated skin area in rats treated with thallium acetate (A), DHT (B), thallium acetate + DHT (C), and restraint + DHT (D). Following treatment with DHT alone, the cutaneous calcinosis is mild, while concurrent treatment with thallium acetate results in formation of a solid, hard plaque of scleroderma-like skin calcinosis. In the remaining 2 animals, no cutaneous lesions are detectable.

FIG. 2. Cross sections through kidneys of rats treated with thallium acetate (A), DHT (B), thallium acetate + DHT (C), and restraint + DHT (D). Only combined treatment with thallium acetate and DHT produces massive selective calcium deposition at the corticomedullary junction line.

* Supported by Nat. Res. Council of Canada (Consol. Gr. 11) and by U. S. Army Med. Res. and Dev. Command, Office of Surgeon General (Contr. DA-49-193-MD-2039).

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TABLE I. Sensitization by Thallium to Dihydrotachysterol Overdosage.

Treatment	Mean final body wt (g)	Calcification (scale 0-3)			
		Cutaneous	Renal	Aortal	Cardiac
Thallium-Ac	122 ± 1.47	0	0	0	0
DHT	104 ± 3.75	1.8 ± .42	0	.3 ± .15	.6 ± .33
Thallium-Ac + DHT	79 ± 3.12	3.0 ± 0	2.8 ± .15	1.1 ± .20	1.3 ± .41
Restraint + DHT	95 ± 2.10	0	0	0	0

sections of specimens fixed in alcohol-formol. The means of these readings, as well as the mean final body weights, are listed in Table I (with standard errors).

Results. Cutaneous lesions were absent in rats treated with thallium alone and moderate in those receiving DHT alone, while combined treatment with both these agents resulted in maximal cutaneous calcinosis in all animals (Fig. 1). No renal lesions were detectable in rats treated with thallium acetate or DHT, alone; but rats given both these compounds exhibited a clearly demarcated zone of intense calcification in the corticomedullary junction zone (Fig. 2).

Thallium acetate also failed to cause calcification in aorta or heart, however, a slight degree of calcium deposition was detectable in these organs, following treatment with DHT alone. The intensity of the aortal calcification was significantly ($P<0.01$) aggravated by concurrent treatment with thallium acetate; but in the heart, this aggravation was not statistically significant ($P = 0.2$).

The sensitization to DHT afforded by thallium acetate could not be ascribed to the stressor effect of the latter, because our earlier findings showed that pretreatment with stress produced nonspecific cross-resistance against DHT-intoxication(5). This was confirmed under the conditions of the present experimental series by the fact that, far from aggravating the syndrome of DHT-intoxication, 24 hours of restraint actually prevented it.

Summary. A single dose of thallium acetate, which in itself produces no detectable organ lesions in the rat, causes severe nephrocalcinosis strictly limited to the corticomedullary junction line if an otherwise nonnephrotoxic dose of dihydrotachysterol (DHT) is administered simultaneously. The DHT-induced calcification in aorta and in traumatized skin regions is greatly aggravated by concurrent treatment with thallium acetate. This sensitizing effect of thallium acetate cannot be ascribed to its stressor action, since under comparable circumstances, exposure to stress (restraint) actually prevents the manifestations of DHT-intoxication.

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Received December 6, 1960. P.S.E.B.M., 1961, v106.

Preliminary Report on a Hemagglutination Test for Entamoebae.* (26355)

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Previous serologic tests for amebiasis have made use of antigens prepared from amoebae grown symbiotically in cultures with mixed or single bacteria from the intestinal tract of man or animals. Such antigens have shown

* Aided by U. S. Public Health Service Grant.