Effect of Exogenous Triiodothyronine on Weight and Composition of the Heart in Rats[1] (37270)

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Thyroxine (T_4) and triiodothyronine (T_3) in high doses cause cardiac hypertrophy. Van Liere, Sizemore, and Hunnell (1) found that 143 μg T_3/kg body weight caused greater relative hypertrophy in the right, than in the left, ventricle; Bartosova *et al.* (2) found no difference in the relative hypertrophy of the two ventricles in response to T_4. Our purposes were to determine whether hypertrophy due to T_3 was indeed greater in the right ventricle, whether this was true of only a particular dose of hormone, and to what degree the hypertrophy might be due to increase in tissues containing hydroxyproline (mainly collagen) since the concentration differs between the two ventricles (2).

Materials and Methods. One hundred and twenty male Sprague-Dawley rats weighing 300–325 g were randomized into control and four treatment groups. L-3,3′,5-Triiodothyronine (Calbiochem) was dissolved in normal saline adjusted to pH 9.0. The four dose levels were 1.2, 6, 30, and 150 μg T_3/kg body weight/day, given subcutaneously for 14 consecutive days to groups of 15 rats (groups 1–4, respectively). A control group (group C) of 15 animals for each treatment group was injected with vehicle only; the controls were later pooled when found not to differ statistically. The rats were weighed every second day and their allotment of Purina laboratory chow pellets was restricted to prevent weight gain or increased at the highest dose of T_3, to prevent weight loss. Within 24 hr of the last injection the rats were anesthetized with 50 mg Nembutal/kg body weight, given intraperitoneally. A 20 gauge needle was inserted into the right ventricle for recording of pulse rate; each recorded value was the mean of several readings at peak inspiration. Hearts were dissected according to the method of Keen (3). The atria were first removed. The right ventricle was then separated by holding the scissors against the septum and cutting around the margin. The papillary muscles were left attached to the free part of the wall. The free portion of the left ventricular wall was separated in a similar manner. Each part was then blotted and weighed and then, after drying, weighed again. Hydroxyproline content was then determined by the method of Prockop and Udenfriend (4). Statistical analysis was based on Student's t test.

Results. A plot of log dose T_3 *versus* heart rate (Fig. 1) yielded a virtually straight line. Heart rate was decreased significantly in group 1 ($p = 0.007$) and increased in groups 3 and 4 ($p < 0.001$).

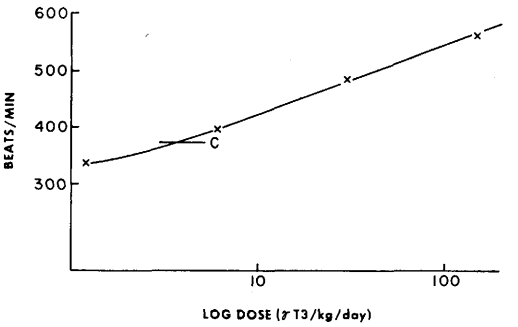

FIG. 1. Relation between heart rate and log dose exogenous T_3 in rats. (C) mean heart rate in 60 control animals; other points are mean values of 15 animals. Heart rate is decreased significantly at the lowest dose.

[1] This investigation was supported by the West Virginia Heart Association.

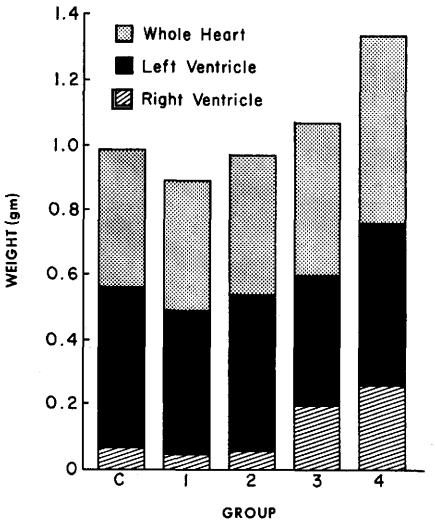

FIG. 2. Wet weight of whole heart and right and left ventricles in control animals (group C) and following injections at 4 dose levels of T_3 (groups 1–4).

Wet heart weight (Fig. 2) was decreased significantly in group 1, ($p < 0.001$) unchanged in 2, and increased in 3 ($p = 0.002$) and 4 ($p < 0.001$). The heart to body weight ratio was decreased in group 1 ($p = 0.003$). The same trends obtained for the individual ventricles as for the whole heart, but the hypertrophy (doses 3 and 4) was more pronounced, proportionally, in the right than in the left ventricle ($p < 0.001$) whereas the atrophy in group 1 was equal in the two ventricles. Dry weight changes paralleled those in wet weight (Table I).

Hydroxyproline concentration in the right ventricle exceeded that in the left (Table I). In the atrophied hearts (Table II, group 1) hydroxyproline concentration increased, at least in the right ventricle ($p = 0.012$); a similar arithmetic difference was seen in the left ventricle but was not statistically significant. In hypertrophy, the hydroxyproline concentration decreased although the absolute amount increased ($p < 0.001$). In summary, the nonhydroxyproline constituents were more responsive in both atrophy and hypertrophy.

Discussion. We corroborate the finding of Van Liere, Sizemore and Hunnell (1) that T_3 can cause relatively greater hypertrophy in the right than in the left ventricle. The atrophy and decrease in heart rate at the lowest dose were unexpected and will therefore require further data for their elucidation. Possibly enough exogenous T_3 was given to shut off secretion of endogenous hormone(s) but not enough to act as replacement hormone at the peripheral tissues.

TABLE II. Percentage Change in Dry Weight and Hydroxyproline (HP) Content of Right and Left Ventricle at 4 Dose Levels of T_3.

		Group			
		1	2	3	4
Left ventricle	Dry wt	−13	−1	+8	+38
	Total HP	−9	−1	+4	+14
	HP	+5	0	−2	−17
Right ventricle	Dry wt	−13	0	+15	+53
	Total HP	−7	−1	+11	+26
	HP	+9	0	−2	−17

TABLE I. Dry Weight of Portions of Heart and Hydroxyproline Content of Dried Ventricles ($M \pm$ SD).[a]

	Group				
	C	1	2	3	4
Dry wt (mg)					
LV	118 ± 11	103 ± 12	117 ± 10	127 ± 16	162 ± 15
RV	32 ± 5	28 ± 4	32 ± 4	36 ± 5	49 ± 6
S	24 ± 4	24 ± 4	25 ± 4	24 ± 3	31 ± 5
HP (γ)					
LV	386 ± 57	352 ± 37	382 ± 57	400 ± 34	442 ± 35
RV	155 ± 17	144 ± 18	153 ± 24	171 ± 20	194 ± 23

[a] LV = left ventricle; RV = right ventricle; S = septum.

The proportionately greater hypertrophy of the right ventricle was not peculiar to the single dose used by Van Liere, Sizemore and Hunnell (approximately our dose 4) but was also seen at one fifth of that dose. The response may be peculiar to T_3. Bartosova *et al.* (2) used T_4 and found that hypertrophy was proportionally equal in the two ventricles; there were however, only eight animals per group in that study. Again, this finding might reflect rate of hypertrophy, and if treatment were prolonged the response in the left ventricle might overtake that in the right.

Summary. Under the conditions of our experiment two doses of T_3 resulted in cardiac hypertrophy which, relatively, was more pronounced in the right ventricle. The changes in heart weight were predominantly a reflection of substances not containing hydroxyproline.

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Received Oct. 23, 1972. P.S.E.B.M., 1973, Vol. 143.