Size of Cardiac Ventricles in Experimental Hyperthyroidism in the Rat[1] (34283)

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Numerous workers have shown that administration of effective doses of a thyroid substance to lower animals, such as dogs (1), rabbits (2, 3), guinea pigs (3), rats (4–9) and mice (10, 11) produce hyperthyroidism with a concomitant cardiac hypertrophy. The consensus is that both ventricles significantly enlarge, but there is considerable question whether they enlarge proportionally the same, or whether one ventricle enlarges proportionally more than the other. No reports could be found in the literature which give the weights of the individual ventricles in cardiac hypertrophy produced by the administration of a thyroid substance. It was deemed worthwhile to study this problem.

Methods and Materials. Male rats of the Sprague-Dawley strain were used. The experiments involved 40 animals: 16 of these served as controls and 24 as experimental animals. They were fed a diet of Purina chow, and kept in an air-conditioned room at a temperature of approximately 75°F. The rats were randomly divided into two groups: those receiving L-3,3'5-triiodothyronine sodium (T_3), and another, the controls, receiving 0.9% sodium chloride. The injections were administered daily for 2 weeks; the T_3 dose was 0.143 mg/kg. Periodically the basal metabolism of the experimental animals was determined in order to ascertain the effectiveness of the thyroid preparation.

On the day following the last injection the rats were weighed and decapitated. The heart was removed, the great vessels were trimmed flush with the surface of the heart, and any remaining pericardium or fat was removed. The blood was expelled from the chambers, the heart was washed free of blood, and the excess moisture removed with filter paper. The heart was weighed, and the weights were recorded in grams of total heart substance per kilogram of body weight.

The hearts were then fixed in a 4% formaldehyde solution. The ventricles were partitioned, following rather closely the technique outlined by Keen (12). The weights of the heart changed slightly during the fixation period. A correction factor was established by dividing the original heart weight by the weight of the heart after fixation. The weight of each ventricle was then recorded. The weights of the ventricles of the experimental animals were compared to the control values, and the percentage of increase determined. The t test was performed to determine significance.

Results. The results are summarized in Table I. Note that administration of T_3 caused a significant cardiac hypertrophy of the whole heart (approximately 32%). The HW/BW ratio was also significantly increased, and, as would be anticipated, each ventricle also showed a significant enlargement. The right ventricle, however, was hypertrophied almost twice as much, on a percentage basis, as was the left. The p value of the difference was 0.002.

The basal metabolic rate was determined periodically by the method of Cline and Watts (13) in 15 experimental and 12 control animals. A few days before these animals were killed the values were 33.5 ± 3.8 and 47.0 ± 7.0 ml of O_2/kg/hr in controls and experimentals, respectively, that is, oxygen use was increased 40.2% ($p<0.001$).

Discussion. Since the functional activity of the heart is appreciably increased in hyper-

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TABLE I. Size of Cardiac Ventricle in Experimental Hyperthyroidism.

No. of animals	(g; M ± SD)				Right ventricle /left ventricle (M ± SD)
	Body wt	Heart wt	Left ventricle	Right ventricle	
Control animals					
16	345 ± 57	1.062 ± 0.192	0.564 ± 0.031	0.198 ± 0.014	0.336 ± 0.061
Experimental animals					
24	286 ± 70	1.402 ± 0.156	0.698 ± 0.094[a]	0.268 ± 0.043[a]	0.388 ± 0.063
	p values		<0.001	<0.001	<0.009

[a] Increase of left ventricle over control, 23.6%; increase of right ventricle over control, 41.4%; the difference, $p = 0.002$.

thyroidism, cardiac hypertrophy would be anticipated. Presumably both ventricles of the heart would be affected, since the increased work load would affect them both. It is worthy of note that recently Cohen *et al.* (11) have demonstrated that hypertrophy of the heart in experimental hyperthyroidism is not due solely to increased functional activity, but is also due to an hormonal factor. The hormone would, of course, affect both ventricles.

The view has been expressed by several workers that in experimental hyperthyroidism the left ventricle shows a greater proportional hypertrophy than the right. As early as 1917 Hering (6), working with hyperthyroid rats, reported that the left ventricle increased more in thickness than did the right. In 1930 Simons and Brandes (1), working with dogs, came to a similar conclusion; they reported that in experimental hyperthyroidism cardiac hypertrophy involves all chambers of the heart, but with a slightly greater proportional increase in the left ventricle. Rake and McEachern (3) a year later, in summarizing the earlier work, emphasized that observers agree that experimental hyperthyroidism produces an enlargement of all the chambers, but with a somewhat greater proportional increase in size of the left ventricle. Apparently no one has seriously challenged these statements.

Cardiac output is significantly increased in hyperthyroidism, and this involves, of course, both ventricles. It might be expected that because of the rapid heart beat and the concomitant increase in systemic blood pressure the left ventricle would hypertrophy proportionally more than the right. Under the conditions of our experiment however, a greater proportional hypertrophy occurred in the right ventricle. This finding, is, indeed, difficult to explain. So far as is known, hyperthyroidism does not produce pulmonary hypertension, such as is found, for example, during hypoxia. It is known that the right ventricle contains a greater concentration of collagen than the left (14, 15). It has been suggested by H. A. Lindsay (personal communication) that this, in some way, might account for the results we obtained. Presently the authors cannot offer a satisfactory explanation for the marked increase in the proportional weight of the right ventricle in experimental hyperthyroidism.

Summary. Experimental hyperthyroidism was induced in male white rats by the administration of T_3. A significant degree of cardiac hypertrophy was produced. The hearts were fixed in a 4% solution of formaldehyde, and the ventricles were partitioned and weighed. The right ventricle showed proportionally a greater degree of hypertrophy (on a percentage basis almost twofold) than the left.

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