LIX. THE EFFECT OF THYROTROPIC HORMONE UPON SERUM CHOLESTEROL.

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It has been shown by a number of workers that the administration of the thyrotropic hormone of the anterior pituitary has a stimulating effect upon the thyroid. The physiological properties and preparation of a highly active and purified extract containing this principle have been recently reported by Anderson and Collip [1934]. Hurxthal and his co-workers in a series of papers [1930; 1933; 1934] have shown that a reciprocal relationship exists between the blood cholesterol and the basal metabolic rate. Recently Cutting *et al.* [1934] have treated the published data on the relationship between basal metabolic rate and blood cholesterol statistically and have confirmed by a regression curve that an inverse relationship exists between these two variables. It has been shown experimentally by Westra and Kunde [1932] using rabbits, and Parhon and Derevici [1931] using dogs, that a decrease in blood cholesterol results from feeding desiccated thyroid and the injection of thyroxine.

In the light of this work, it seemed of interest to investigate the effect of the thyrotropic hormone upon serum cholesterol.

Methods.

A group of 15 adult rats weighing between 280 and 320 g. was chosen for the experiment. During the injection period, 3 or 4 rats were bled by heart puncture every second day. Successive samples were taken from each animal at 6-day intervals, in order to minimise the effects of haemorrhage. Between 1.2 and 1.5 ml. of blood were removed each time and 0.5 ml. of serum was used in the estimation of cholesterol, which was carried out by the method of Sackett [1925]. This amount of serum was found necessary on account of the low value for serum cholesterol in the rat. The normal level for cholesterol was obtained from a group of 12 rats and these were also bled at intervals of 6 days on different occasions to show that the removal of this quantity of blood did not interfere with the level of cholesterol.

The rats received twice daily 0.5 ml. of an active thyrotropic extract which was shown to contain 50 units of the hormone per ml. as assayed on the hypophysectomised rat.

Results.

The results are shown in Table I. The normal values for serum cholesterol of rats varied between 64 and 75 mg. per 100 ml. with an average value of 70 mg. per 100 ml. Upon injection of the thyrotropic hormone, the serum cholesterol decreased markedly, reaching its lowest level on the 8th to 10th day of injection and then returning to the normal level or slightly above in the course of 2 weeks. The values are expressed graphically in Fig. 1. This graph has a striking re-

ciprocal relationship to the basal metabolic rate curves shown by Pugsley *et al.* [1934] in their study of the effect of thyrotropic hormone upon creatine and creatinine excretions of normal and hypophysectomised rats.

Table I. *The effect of thyrotropic hormone upon the serum cholesterol of rats.*

The values are expressed in mg. per 100 ml. of serum.
0.5 ml. b.i.d. Extract 2 intraperitoneally for 40 days.

Days	No. of determinations	Maximum	Minimum	Average
Control	12	75	64	70
2	4	60	57	59
4	4	60	49	54
6	4	64	48	59
8	4	64	64	64
10	3	55	40	46
12	6	60	43	49
14	4	58	53	54
16	3	54	51	53
18	4	74	60	66
20	4	74	52	66
22	3	77	54	68
24	4	80	66	75
26	4	95	71	82
30	3	96	69	81
32	3	95	66	83
34	3	74	68	72
36	3	83	64	74
40	4	87	63	73

Fig. 1. The effect of thyrotropic hormone upon the serum cholesterol of rats.

The serum cholesterol has also been studied in dogs after intravenous and intraperitoneal injections of the thyrotropic hormone. The results are shown in Table II. In dog no. 1 it is seen that the injection of a potent thyrotropic extract caused a marked decrease in the serum cholesterol. This is confirmed in dog no. 2, using the extract employed in the experiments on rats. When the injections were discontinued the cholesterol values returned to the control level within 2 weeks. With continued injections, as is shown in dog no. 1 B, the same decrease in cholesterol was found, but the values did not return to the control level as rapidly as they did in the chronically-treated rats. The injections were continued for 68 days and the serum cholesterol was determined every second day; during this time the values ranged between 125 and 145 mg. per 100 ml. In dog no. 1 C it is shown that boiling the thyrotropic hormone at p_H 6.0 for 30 minutes in an open flask completely destroys its effect in lowering the serum cholesterol.

Table II. *The effect of thyrotropic hormone upon the serum cholesterol of dogs.*

The values are expressed in mg. per 100 ml. of serum.

Days	Dog no. 1	Dog. no. 2	Dog no. 1B	Dog no. 1C	Dog no. 3
Control	340	218	275	273	240
Control	342	220	272	270	240
2	333	218	208	270	240
4	253	160	168	274	240
6	200	155	135	265	218
8	171	137	120	272	222
10	163	130	114	—	220
12	—	120	114	—	222
16	—	125	100	—	218
20	—	177	107	—	240
24	273	218	145	—	—
28	—	—	141	—	—
38	—	—	133	—	—
48	—	—	130	—	—
68	—	—	123	—	—

Dog no. 1. Male. Wt. 16 kg. 10 ml. b.i.d. Extract 1 intravenously for 10 days.

Dog no. 2. Male. Wt. 15 kg. 5 ml. b.i.d. Extract 2 intraperitoneally for 12 days.

Dog no. 1B. Male. Wt. 16 kg. 5 ml. b.i.d. Extract 2 intravenously for 68 days.

Dog no. 1C. Male. Wt. 16 kg. 10 ml. b.i.d. Extract 1 intravenously (boiled) for 8 days.

Dog no. 3. Female. Thyroparathyroidectomised-hypophysectomised. Wt. 12 kg. 5 ml. b.i.d. Extract 2 intraperitoneally for 20 days.

The effect of the thyrotropic hormone upon the serum cholesterol of a thyroparathyroidectomised-hypophysectomised dog has been studied (dog no. 3). The completeness of these operations has not been established as yet. However, the thyroparathyroidectomy appears to be complete, since the serum calcium showed a marked decrease following the operation (11.6 to 7.8 mg. per 100 ml.). The animal received parathyroid hormone (Eli Lilly and Company) for some time, but during the administration of the thyrotropic hormone no parathyroid hormone was given. The dog was in good health and showed no symptoms of tetany during this time. The serum calcium which was also followed ranged between 7.0 and 8.0 mg. per 100 ml. In this dog no significant decrease in the cholesterol was observed as a result of the injections. This observation is in agreement with the reports of Verzar and Wahl [1931] and others that the thyrotropic hormone does not function in thyroidectomised animals.

SUMMARY.

The intraperitoneal injection of the thyrotropic hormone caused a marked decrease in the serum cholesterol of rats and dogs.

The serum cholesterol curve shows a reciprocal relationship to the basal metabolic rate curve of rats receiving chronic injections of the thyrotropic hormone.

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