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Effect of Thyrotropic Hormone on Blood Cholesterol of Thyroidectomized Rabbits.

KENNETH B. TURNER AND ARLENE DELAMATER.

From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York City.

There is general agreement that the administration of thyroid substance produces a lowering of the cholesterol level in the blood of man and experimental animals. As might be expected, this drop occurs in the absence of the thyroid gland in man[1] and in rabbits.[2]

The thyrotropic hormone of the anterior pituitary is also capable of causing a fall in the blood cholesterol.[3] The purpose of the present investigation was to determine whether this action of the hormone persisted in rabbits after the complete removal of the thyroid glands.

Dutch belted rabbits from 4 to 6 months old were fed 1 g of crystalline cholesterol thrice weekly mixed with moistened grain for an average of 8 months previous to and throughout the experimental period. The whole blood cholesterol of each animal was determined by the method of Bloor, Pelkan, and Allen[4] weekly during the preliminary period and every 2 days after the experiment began.

Five rabbits were used as controls. Eleven were operated upon and the thyroids removed under ether anesthesia from 1 to 4 months before injections were started. At the end of the experiment, an autopsy was performed. Regenerated thyroid tissue is ordinarily obvious on inspection because of its brownish red color that is sharply in contrast to the red of the muscles and other structures. In case of doubt a section was made for microscopic examination. It was found that the thyroids had been completely removed in 6 animals, but in 5 the thyroidectomy had been incomplete and more or less regeneration of thyroid tissue had taken place. These have been designated as "partially thyroidectomized".

The thyrotropic hormone was obtained through the courtesy of the Schering Corporation. It was injected subcutaneously daily for 10 to 14 days in doses of 9 mg per day except for 4 rabbits (Nos. 368, 390, 393, 394) that were given 3 mg doses.

Each rabbit was weighed before and after the series of injections.

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1 Blumgart, H. L., and Davis, D., *Endocrinology*, 1934, **18**, 693.

2 Turner, K. B., Present, C. H., and Bidwell, E. H., *J. Exp. Med.*, 1938, **67**, 111.

3 Fenz, E., and Zell, F., *Klim. Wchnschr.*, 1936, **15**, 1133.

4 Bloor, W. R., Pelkan, K. F., and Allen, D. M., *J. Biol. Chem.*, 1922, **52**, 191.

TABLE I.
Effect of Thyrotropic Hormone on Blood Cholesterol.

		Weight		Blood Cholesterol														
		Before hormone	After hormone	Avg during control mo.	Days of hormone injection (mg/100 cc)							Max. decrease,	Avg during hormone inj.,	Days after hormone (mg/100 cc)						
Rabbit	Sex	kg		(mg/100 cc)	2	4	6	8	10	12	14	%	(mg/100 cc)	2	4	6	8	10	12	14
Intact																				
368*	M	1.5	1.1	591	467	521	527	549	—			21	516	503	(died)					
390*	M	2.0	1.9	491	515	410	481	471	—			14	469	444	—	358	—	—	—	409
378	F	2.1	1.7	477	319	346	356	376	—			33	349	366	(died)					
388	F	1.8	1.2	595	—	361	398	391	—			39	383	409	621	519	(died)			
411	M	2.4	2.4	656	525	410	456	421	252	—		62	413	268	268	207	228	164	156	124
			Avg	562								45	426							
Partially thyroidectomized																				
393*	M	1.9	1.7	607	527	487	417	404	—			33	459	433	—	485	—	—	—	—
387	F	2.3	2.2	683	446	513	467	322	—			53	437	336	700	597	700	—	630	—
400	M	1.8	1.6	603	521	565	600	625	670	—	450	25	572	625	575	381	—	520	550	430
415	M	2.1	1.9	456	306	312	262	236	200	—	250	56	261	237	248	316	—	344	382	408
424	M	1.6	1.5	345	535	286	241	262	211	139	—	60	279	76	135	238	253	204	174	132
			Avg	539								49	402							
Thyroidectomized																				
394*	M	1.8	1.8	341	431	312	313	278	—			18	334	325	—	309	—	—	—	371
336	F	2.0	1.9	470	352	476	505	446				25	445	433	424	515	726	—	519	—
408	F	1.6	1.5	460	506	450	348	284	475			38	413	220	214	230	213	230	214	338
412	M	1.8	1.6	502	515	284	338	340	310	318	—	43	351	261	310	420	—	500	—	565
452	F	1.5	1.6	406	375	342	228	264	311	—		44	304	315	350	421	—	357	—	—
457	M	1.8	1.7	450	371	368	226	272	211	—		53	290	318	375	347	—	383	—	—
			Avg	438								41	356							

*Received 3 mg doses of hormone

The results are given in Table I. The average level of blood cholesterol during the month preceding the administration of the hormone is indicated for each rabbit. A hypercholesterolemia due to the cholesterol feeding was present in each instance. It is apparent that the injection of thyrotropic hormone produces a fall in the level of cholesterol in the blood regardless of the presence or absence of thyroid tissue. The effect is less marked when 3 mg of the hormone is given than with 9 mg per day.

The drop in blood cholesterol may be summarized:

	Avg during Control month, mg	Avg during hormone inj., mg	Decrease in avg, %	Max. decrease, %
Intact rabbits	562	426	24	14-62
Partially thyroidectomized	539	402	25	25-60
Thyroidectomized	438	356	19	18-53

Following the period of hormone injection the blood cholesterol tended to rise. In rabbit No. 411 of the control group, however, the cholesterol fell progressively after the injections were stopped. At autopsy the thyroids were 3-4 times normal size and extremely vascular. Unfortunately no sections were made.

The mechanism by which the thyrotropic hormone lowers the blood cholesterol in the absence of the thyroid gland remains to be elucidated. It has recently been shown[5] that the increase in oxygen consumption caused by the thyrotropic hormone also persists after thyroidectomy.

It is of interest that the hormone had little or no effect on the weight of the rabbits whose thyroids had been completely or partly removed. In 3 of the 5 intact animals a substantial weight loss occurred and was followed by death 2 to 7 days after the hormone was discontinued.

Summary. Thyrotropic hormone produces a fall in the blood cholesterol of hypercholesterolemic rabbits regardless of the presence or absence of the thyroid glands.

[5] Billingsley, L. W., O'Donovan, D. K., and Collip, J. B., *Endocrinology*, 1939, **24**, 63.