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The Relation of Thyroid to Creatine and Creatinine Excretion in the Rat.*

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It is generally stated that creatinuria accompanies hyperthyroidism in mammals and that there is a decrease in the excretion of creatine with hypothyroidism if the mammal excretes creatine normally.[1, 2, 3] Experimental studies on the creatine-creatinine excretion have been made on normal and hyperthyroid rats but none to our knowledge have been made on the thyroidectomized rat. This preliminary note on the creatine-creatinine excretion in normal and thyroidectomized rats is part of a comprehensive study being undertaken on the relationship of the endocrines to creatine-creatinine metabolism.

Methods. Adult male rats weighing about 250-350 g, of the Sprague-Dawley strain, were used and were fed a diet of Purina chow *ad lib.* They were kept in individual metabolism cages and 24-hour samples of urine were collected under toluol. The modified Folin[4] methods for determining creatine and creatinine were used. The amounts of creatine and creatinine excreted during 24-hour periods were expressed in millimoles per kilo of rat.

Experimental. (1) Determinations of creatine and creatinine were made on 5 24-hour urine samples from each of 5 thyroidectomized and 4 control rats over each of 2 2-week periods. The normal level of excretion of these substances was determined from 8 samples for the previous 2 weeks. The control group was subjected to a mock operation at the time the others were thyroidectomized. A summary of the data, presented in Table I, demonstrates that there is a reduction in the excretion of creatine in thyroidectomized rats which is not shown by the controls and that there is more of a tendency for the excretion of creatinine to increase in the thyroidectomized animals than in those subjected to a mock operation.† It is

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1 Kendall, E. C., *Thyroxine,* 1929, Chem. Catalogue Co.

2 Hunter, A., *Creatine and Creatinine,* 1928, Longmans, Green and Company.

3 Pugsley, L., Anderson, E., and Collip, J. B., *Biochem. J.,* 1934, **28**, 1135.

4 Folin, O., *J. Biol. Chem.,* 1914, **17**, 469.

† The significance of these findings is increased by recent data obtained by Mr. Glaser. He injected 10-20 mg of creatine into 2 thyroidectomized and 2 control rats and recovered approximately 40% less of this excess creatine from the urine of the thyroidectomized than from the control animals. The injection experiments were repeated using creatinine but the excretion of an excess of this substance was unaffected by thyroidectomy.

TABLE I.
Millimoles per kg of Creatine and Creatinine Excreted in 24 Hours by White Rats During a 2-week Period Before, and During a 4-week Period After Thyroidectomy or After Mock Operation Without Thyroidectomy.

	Before operation 2 weeks	After thyroidectomy	
Rat No.	Avg 8 samples creatine millimoles	First 2 weeks Avg 5 samples creatine millimoles	Second 2 weeks Avg 5 samples creatine millimoles
1	.122	.050	—
2	.116	.052	—
3	.082	.054	.048
4	.089	.040	.045
5	.092	.061	.064
Avg	.100	.051	.052
		After mock operation	
6	.088	.076	.070
7	.091	—	.142
8	.118	.105	.130
9	.163	.138	.162
Avg	.113	.106	.126
		After thyroidectomy	
	Avg 8 samples creatinine millimoles	Avg 5 samples creatinine millimoles	Avg 5 samples creatinine millimoles
1	.232	.281	—
2	.180	.226	—
3	.255	.255	.296
4	.254	.255	.263
5	.257	.243	.273
Avg	.236	.252	.277
		After mock operation	
6	.268	.258	.246
7	.238	—	.275
8	.246	.258	.244
9	.222	.235	.240
Avg	.243	.250	.251

possible that the decrease in the excretion of creatine by the thyroidectomized animals is due at least in part, therefore, to a reversible creatine-creatinine reaction.

(2) The 5 thyroidectomized rats were injected with 0.25 mg of thyroxin for 4 days. The averaged data obtained on 3 of these rats studied simultaneously are illustrated in Fig. 1. These data show the effect thyroxin had on all 5 rats. In every case there was a marked increase in the excretion of creatine accompanied by a loss of body weight. The slight decrease in the excretion of creatinine observed in the averaged data 2 to 5 days after the last injection of thyroxin also may be significant.

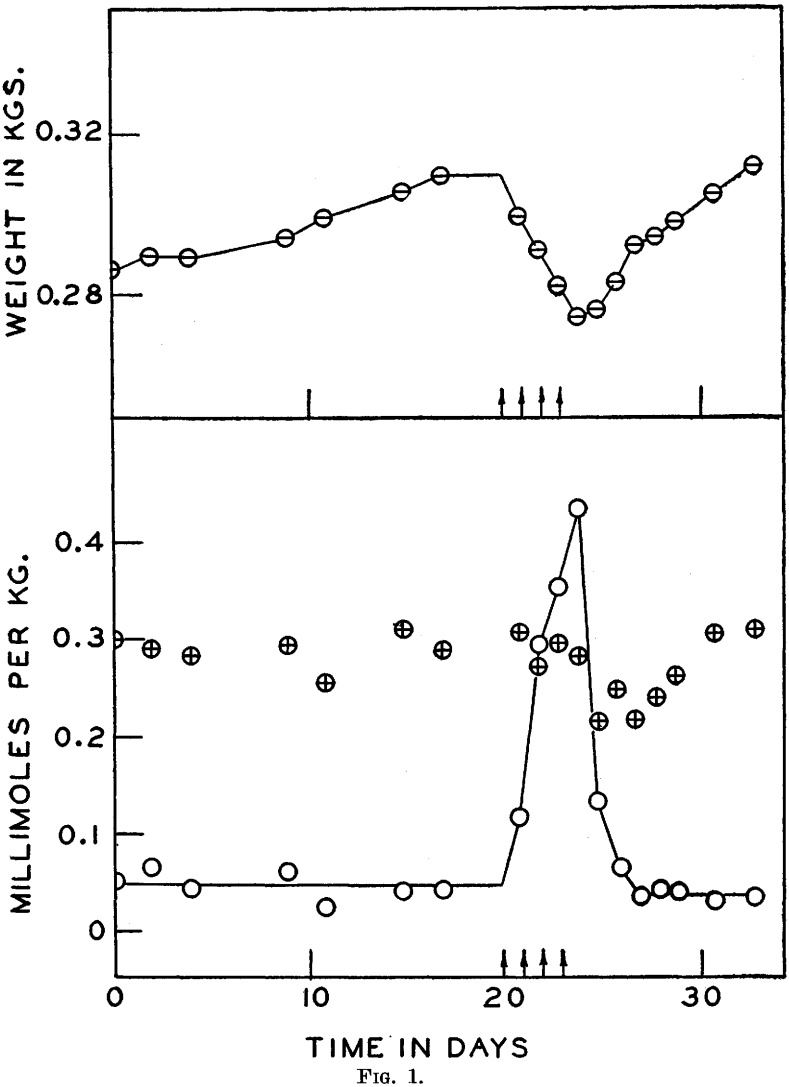

FIG. 1.

The average weights in kilograms ⊖ of 3 thyroidectomized rats are plotted against time in days. The average millimoles of creatinine ⊕ and of creatine ○ excreted per kilogram of body weight in 24 hours are plotted against time in days. 0.25 mg of thyroxin were injected in each rat each day for 4 days, indicated by the arrows.

Summary. Preliminary data demonstrate that (1) thyroidectomy decreases creatine excretion and suggests that this decrease always may be accompanied or followed by an increase in creatinine; (2) injection of thyroxin into thyroidectomized rats increases the excretion of creatine with loss in body weight followed by a slight and probably significant decrease in the excretion of creatinine.