

15993

Effect of Hypothyroidism and Hyperthyroidism on Mammalian Skeletal Muscle.*

R. DIAZ-GUERRERO, J. D. THOMSON, AND H. M. HINES.

From the Department of Physiology, State University of Iowa, Iowa City.

Observations on clinical hyperthyroidism frequently mention as part of the syndrome asthenia, dystrophy and fine tremors of voluntary muscle. Remission of some of these symptoms often follows thyroidectomy. Pathological changes have been observed in such muscles.¹ Creatinuria is often present,² further indicating the existence of some muscular disorders. The present study reports the effect of hypo- and hyperthyroidism on the weight, strength and fatigability of skeletal muscle of the albino rat.

Methods. A total of 150 albino rats closely matched as to initial body weight, age and sex, was used in this study. One group of adult rats was made hypothyroid by including thiouracil in the diet³ in amounts sufficient to lower the B.M.R. by approximately 20% (2 g thiouracil per kg powdered Purina Laboratory Chow). The hyperthyroid state was produced in one group by subcutaneous injection of 1.5 to 2.0 mg thyroxin twice a week. A third group served as untreated controls. Treatment was carried out for an average of 60 days before measurements were made of muscle weight and strength. The strength of the intact gastrocnemius-soleus muscles was determined by measuring the maximal isometric tension response of the muscles to slightly supermaximal condenser discharge stimuli applied to the tibial nerve with the animal under light ether anesthesia. The techniques that were employed for strength measurements have been described in detail elsewhere.⁴

For the fatigue studies 35-day-old rats were divided into 3 groups. One group was given subcutaneous injections of thyroxin twice a week in amounts of 6 mg per kg body weight. A second group was reared on the thiouracil diet and a third group served as their untreated controls. Fatigue studies were made 90 days later on these animals while they were under light ether anesthesia. This was done by optically recording the isometric tension response of the gastrocnemius-soleus group to condenser discharge stimuli at slightly supermaximal intensity applied at the rate of 120 per second to the tibial nerve and induction shocks applied directly to the muscles at the rate of 120 per second. The records were analyzed for 2 indices of fatigue. The tensions maintained at 5 and 10 seconds after the onset of stimulation were calculated as per cent of the earlier maximal tensions and the area under the first 10 seconds of the tension curve was measured planimetrically from optical records.

Results. No significant difference was found (Table I) between the weight and strength of control and thiouracil treated animals. The thyroxin treated animals exhibited muscular weakness. This was shown by the findings of lower total tension, reduced tension per g of muscle, less tension per unit of body weight and a slightly lower ratio of muscle weight to body weight. Similar results were obtained in the studies on the younger group of animals which were under treatment for longer periods of time. Isometric tetanus tension elicited by nerve stimulation declined more rapidly in the hyperthyroid animals than in their controls. This was evidenced (Table II) by a reduction in the area of the tension curve and by a

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

¹ Alkanozzy, M., *Deutsches Arch. f. Klin. Med.*, 1898, **61**, 118.

² Palmer, W. W., Carson, D. A., and Sloan, L. W., *J. Clin. Invest.*, 1929, **6**, 597.

³ Barker, S. B., *Endocrinology*, 1946, **29**, 234.

⁴ Hines, H. M., Thomson, J. D., and Lazere, B., *Am. J. Physiol.*, 1942, **137**, 527.

TABLE I.
Average Values, with Standard Errors, for Effect of Thyroxin and Thiouracil on Weight and Strength of Muscle.

	Control		Thyroxin		Thiouracil	
No. of animals	54		45		51	
Body wt before	173		171		170	
" " after	269		240		248	
Muscle* wt						
× 100	0.650 ± 0.007		0.622 ± 0.007		0.676 ± 0.008	
Body wt						
Total muscle* strength (g isometric tension)	3245 ± 84		2599 ± 149		3098 ± 90	
Tension per g muscle*	1825 ± 35		1629 ± 33		1806 ± 33	
Total muscle* tension						
Body wt	11.87 ± 0.253		10.26 ± 0.268		12.12 ± 0.162	

* Gastrocnemius-soleus.

TABLE II.
Average Values, with Standard Errors for Area Under Fatigue Curve, and Per Cent of Maximal Tension Remaining at 5 and 10 Seconds Through Direct and Indirect Stimulation.

Treatment	Area under 10 second fatigue curve muscle activated through		Nerve stimulation % max. tension		Muscle stimulation % max. tension	
	nerve cm ²	muscle cm ²	5 sec %	10 sec %	5 sec %	10 sec %
Thyroxin	50.7 ± 1.80	82.0 ± 2.24	27.9 ± 0.97	11.3	78.3	50.9
Control	75.4 ± 1.81	106.1 ± 2.27	44.6 ± 1.15	14.1	75.9	51.6
Thiouracil	63.3 ± 2.24	104.0	36.4 ± 1.54	11.8	76.8	53.8

lower per cent of tension existing after 5 seconds of stimulation. The thiouracil treated animals were inferior to their controls in respect to the maintenance of tension in muscle during motor nerve stimulation. No significant differences were noted between the three groups for the per cent of maximal tension decreases after 5 seconds of direct muscle stimulation. However, the tension area for direct muscle stimulation was significantly lower in the thyroxin treated than in the control animals.

Discussion. The evidence on the whole indicates that the hyperthyroid state is associated with some degree of muscular weakness and increased susceptibility to fatigue. The failure to maintain tetanus tension from nerve stimulation together with normal response to direct stimulation suggests that the factor of neuromuscular transmission may be involved. The hypothyroid condition resulting from thiouracil administration was accompanied by normal muscle weight and strength relationship except for a slightly more rapid

decline in the tetanus tension elicited by motor nerve stimulation. It is to be pointed out that these studies deal only with the capacity of the muscles to develop and maintain tension in response to nerve stimulation and are not concerned with the stimulus pattern that is utilized in the natural activation of the muscles in reflex and voluntary activity. The asthenia that might result from subnormal activation would not be apparent in this type of study.

Summary. Albino rats were made hypothyroid by treatment with thiouracil and hyperthyroid by administration of thyroxin. After 60 days of treatment, gastrocnemius-soleus muscles of thyroxin treated animals showed weakness and increased susceptibility to fatigue through motor nerve stimulation. Thiouracil treatment for a like period of time resulted in no loss of muscle weight or strength, but did produce a slight increase in susceptibility to fatigue by indirect stimulation.