Suarez, R. M., Jr., and Nelson, E. M., *J. Lab. and Clin. Med.*, 1946, v31, 1294.

8. Spies, T. D., *South. Med. J.*, 1946, v39, 634.

9. Jones, E., Worden, H. F., and Darby, W. J., *J. Lab. and Clin. Med.*, 1947, v32, 387.

10. Nichol, C. A., and Welch, A. D., PROC. SOC. EXP. BIOL. AND MED., 1950, v74, 52.

11. ———, *ibid.*, 1950, v74, 52.

12. Broquist, H. P., Stokstad, E. L. R., and Jukes, T. H., *J. Biol. Chem.*, 1950, v185, 399.

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Effect of Muscular Exercise on Circulating Thyroid Hormone.* (21059)

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Recent studies by many investigators have dealt with the effect of various injurious agents and stimuli on the uptake of I^{131} by the thyroid gland. For example, Bogoroch and Timiras(1) found a consistent decrease in the uptake of I^{131} by the thyroid glands of rats after the injection of formalin or transection of the spinal cord. They also studied the effect of forced muscular exercise on the uptake and found that in one group there was no significant change, while in a second group there was a significant depression. Increased secretion of thyroid hormone on exposure to cold has been demonstrated in rats by Dempsey and Astwood(2) and increased peripheral utilization of the hormone in rats by Rand(3) and by Bondy(4), and in man by Ingbar and Kleeman(5). Bondy also found in rats that 2 hours of swimming caused a pronounced fall in serum protein bound iodine.

The present study was undertaken to determine the effect of muscular exercise in man on the level of circulating hormone and on the rate of disappearance of injected l-thyroxine labeled with radioactive iodine.

Procedure. 1) *Moderate exercise.* One female and 5 male medical students and physicians in good health varying in age from 20 to 36 years walked 14 miles in 4 to 4½ hours. In the first 2 subjects the serum butanol extractable iodine (BEI) concentration was determined at the start, after 7 miles, at the end of the walk, and 5 hours and 16 hours after the end of the walk. Control BEI determinations were made on the same subjects at the same hours during an average day. The second 2 subjects received an injection of 40 μc of radio-thyroxine 5 days before the walk. Serum radioactivity was determined at 9 a.m., 12 N., and 5 p.m. daily for 16 days. On the day of exercise the serum radioactivity was estimated and BEI's determined at the start, at the end of 7 miles, at the end of 14 miles and the following day. The third 2 subjects walked the same distance and BEI determinations performed at the beginning and end of the exercise and on the following morning. 2) *Severe brief exercise.* Six healthy male subjects swam at maximum speed for 15 minutes. All were good swimmers but had not swum for several months and were acutely exhausted at the end. Serum protein bound iodines were estimated before and at the end of the swimming.

Methods. 1) Butanol extractable iodine was measured by the method of Man(6). 2) The radio-thyroxine disappearance curves were performed according to the method of Sterling(7), the subjects being given saturated solution of potassium iodide to minimize re-

TABLE I. Serum BEI's of Subjects Walking 14 Miles (γ %).

Subject	B.	L.	S.	J.	H.	T.
Start	6.8	5.9	4.1	4.7	5.0	4.8
Midpoint, 2 hr	6.4	5.3	4.0	5.2		
End	6.5	5.6	4.4	3.5	4.9	5.2
5 hr after exercise	6.9	6.0				
Next a.m.	6.4	5.9	3.3	4.3	5.9	4.7
△ end-start	−.3	−.3	+.3	−1.2	−.1	+.4

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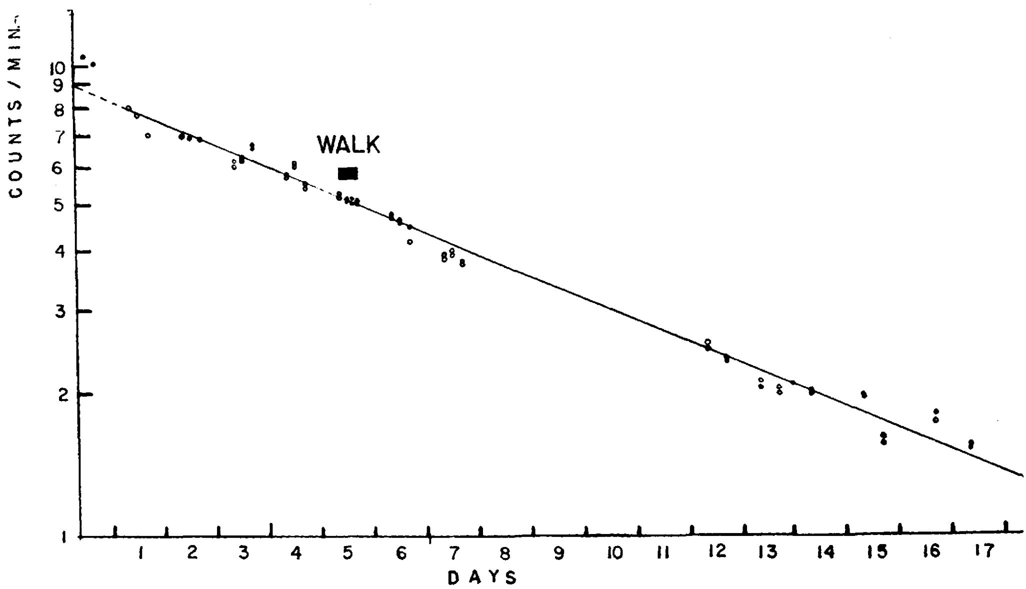

FIG. 1. Radio-thyroxine disappearance curve of subject J. Abscissa = days after injection of radio-thyroxine. Ordinate = counts per minute per cc of plasma.

utilization of radioiodide liberated from thyroxine breakdown. 3) The alkaline ash method of Barker, Humphrey and Soley(8) was used for the determination of protein-bound iodine.

Results. The results obtained in the 6 subjects who walked 14 miles are given in Table I. The reproducibility of the BEI method has been statistically analyzed. For a range of 2 to 8 γ % the difference between the means of two sets of duplicates must be 1 γ % to indicate a significant change ($p = 0.01$). Only one subject, J., showed a significant fall after exercise; but this concentration was not significantly below the BEI determined the following a.m. The BEI failed to change during an average day in the first 2 subjects.

The normal slope of the thyroxine degradation curve showed no change on the day of exercise in either subject. Fig. 1 represents the thyroxine degradation curve of one of the 2 subjects given radio-thyroxine.

In Table II the protein bound iodines before and after swimming are presented. No significant change was observed.

Blood hemoglobin and hematocrit and serum protein concentration were estimated in some of the subjects to rule out any change due to hemodilution or hemoconcentration. No significant change was found.

Discussion. The conception has been entertained that acute metabolic demands of the body may increase the peripheral utilization of thyroid hormone. In the present study muscular exercise resulted in no evident change in the concentration of circulating thyroid hormone. The stable hormone concentration could not be attributed to increased secretion counterbalancing increased removal from the blood in view of the unaltered radio-thyroxine disappearance curves. Within 2 days of injection of radio-thyroxine the decrease in serum radioactivity formed a straight line on semilogarithmic plot representing the rate of degradation of the hormone(7). With the method used a measurable change in the slope of the disappearance curve should be produced by about a 20% increase in the rate of hormone degradation on the day of exercise.

TABLE II. Serum PBI's of Subjects Swimming 15 Minutes (γ %).

Subject	A	B	C	D	E	F
Start	7.0	7.5	6.5	7.7	7.2	6.5
End	6.5	8.4	8.4	6.8	5.4	6.1
Δ end-start	–.5	+.9	+1.9	–.9	–1.8	–.4

The fact that in the present study no change in thyroid metabolism occurred may indicate that a much more prolonged change in the metabolic needs of the body is required in order to alter thyroid function. Previous studies on cold exposure have demonstrated increased rate of removal of circulating thyroid hormone. However, maintenance of body temperature is a major function of thyroxine. Need for the calorigenic action of the hormone on exposure to cold may prove to be the most consistent means of increasing the utilization of thyroxine. In the rat experiment of Bondy and Hagewood(4) the temperature of the water (27°C), rather than the muscular exercise, may have been enough to account for the fall in protein bound iodine. Tan *et al.* have shown that the survival time of rats swimming in water which is below body temperature is limited by the ability of the rat to maintain body temperature at its normal level(9). Muscular exercise itself increases heat production and this may militate against increasing the rate of utilization of thyroid hormone in the present experiments by increasing the body temperature. Whether or not stimuli other than cold do affect the rate of the peripheral metabolism of thyroid hormone remains to be determined. Previous studies of the effect of injurious agents have dealt mainly with the thyroidal uptake of I^{131} rather than with the rate of disappearance of circulating hormone. The uptake of I^{131} may be influenced by many factors other than the rate of utilization of thyroxine, such as previous diet, adrenal cortical, pituitary and renal function.

Summary. Muscular exercise in human subjects produced no alteration in peripheral utilization of thyroid hormone as measured by concentration of circulating hormone and by rate of disappearance of injected radiothyroxine.

1. Bogoroch, R., and Timiras, P., *Endocrinol.*, 1951, v49, 548.

2. Dempsey, E. W., and Astwood, E. B., *ibid.*, 1943, v32, 509.

3. Rand, C. G., Riggs, D. S., and Talbot, N. B., *ibid.*, 1952, v51, 562.

4. Bondy, P. K., and Hagewood, M. A., PROC. SOC. EXP. BIOL. AND MED., 1952, v81, 328.

5. Ingbar, S., and Kleeman, C. R., unpublished data.

6. Man, E. B., Kydd, D. M., and Peters, J. P., *J. Clin. Invest.*, 1951, v30, 531.

7. Sterling, K., Lashof, J. C., and Man, E. B., *ibid.*, in press.

8. Barker, S. B., Humphrey, M. J., and Soley, M. H., *ibid.*, 1951, v30, 55.

9. Tan, E. M., Hamson, M. E., and Richter, C. P., *Fed. Proc.*, 1954, v13, 150.

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Effect of ACTH on Strength of Intestinal Anastomoses in Dogs. (21060)

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Since the original observations by Ragan (1) concerning the retardation of wound healing in patients by ACTH, several studies have been done dealing with this phenomenon. The investigations of Ragan(2), Spain(3), and others in rabbits and mice indicate that ACTH retards the healing of wounds. Recent experiments on skin wounds in guinea pigs(4) and rats(5), and on skin wounds and cardiovascular suture lines in dogs(6,7) failed to demonstrate significant differences in the healing of wounds of control animals and those treated with ACTH or cortisone. The conflict in these experimental results may be attributable to differences in the species of experimental animal, the particular tissue studied, or to the dosage of the hormone used.

The effect of ACTH and cortisone on anastomoses in the gastrointestinal tract is important for obvious reasons. Great caution has been advocated in the use of these agents in the presence of healing anastomoses(8). In one clinical series unspecified as to detail 4 of 10 cases with intestinal anastomoses