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Creatine Excretion in Artificial Hyperthyroidism.

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An attempt was made to produce creatinuria in 3 individuals by the ingestion of thyroid extract. Palmer[1] has recently reported that creatine is excreted in the urine of patients suffering from hyperthyroidism and that under iodine medication this excretion tends to disappear. Creatine determinations were made by the method of Folin.[2] Tests for acetone and diacetic acid in the urine were negative. The first subject, an arterio-sclerotic individual of 63, having an initial basal metabolic rate of —22, was placed on a meat-free diet with 1.25 gm. of protein per kilogram of body weight. After observing his creatinine excretion he received gr. 19 of thyroid extract (Armour) over a 6-day period, then gr. 6 daily over a 4-day period, then gr. 9 daily for 8 days, and finally gr. 6 daily for 16 days. Creatine appeared in the urine on the second day of thyroid administration, disappeared on the twelfth, and then rose to a maximum excretion of 483 mg. on the twentieth day of the experiment. This coincided with a B.M.R. of +33. When the dose of thyroid was decreased to gr. 6 daily and 1 cc. of Lugol's solution was given twice a day for 7 days the creatine excretion fell to 100-

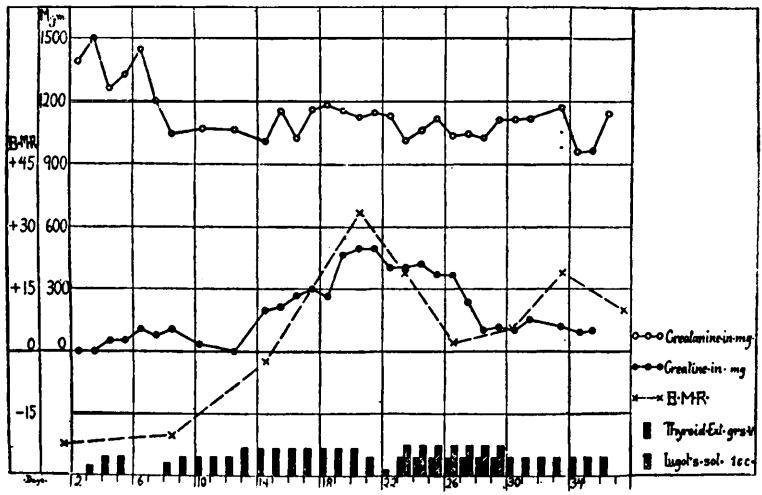

CHART. Effects of Thyroid Extract and Lugol's Solution on Excretion of Creatinine and Creatine in Urine. The blocked and hatched areas in the abscissa represent doses of thyroid and of Lugol's solution.

150 mg. a day. This was not an iodine effect, however, as continued administration of thyroid without iodine was not sufficient to maintain metabolism at its previous high levels or to increase creatine excretion. The average daily excretion of creatinine amounted to 1350 mg. During the experiment this fell to a level averaging 1050-1100 mg. The complete figures are shown in the accompanying chart.

The second subject, a normal male of 29, having an initial B.M.R. of —5, on an unrestricted diet, took daily doses of thyroid extract (Burroughs and Wellcome) increasing from gr. 10 to gr. 35. Urine collections were irregular but there was a creatine excretion of 36-221 mg. per day in the earlier part of the experiment without significant changes in the excretion of creatinine. Observations were discontinued before the B.M.R. was materially elevated.

The third subject was a normal male of 31. The initial B.M.R. was +4. He was placed on a diet similar to that given subject 1, and took thyroid extract (Armour) in daily doses of gr. 5 for 6 days, gr. 6 for 1 day, gr. 9 for 3 days, and gr. 12 for 10 days. The creatinine excretion was constant during 18 days. Creatine appeared in the urine on the third day of medication, disappeared on the sixth day, reached a maximum of 178 mg. on the eighth day, and finally disappeared on the fifteenth day, not to reappear during the next three days. The B.M.R. was at its height, +23, at this time. The effect of iodine medication on creatinuria could not, therefore, be observed.

Creatinuria, then, can be produced in the human by the ingestion of thyroid extract but it can not be maintained from day to day unless a severe intoxication be developed. The disappearance of creatine from the urine in the earlier part of the experiment in subjects 1 and 3, and its complete disappearance in the case of subject 3 when the basal metabolism was at its height is an unexplained observation which should be investigated. As there was no correlation between the dose of thyroid and the creatine excretion it was probably not due to the presence of creatine or its precursors in the thyroid extract. It suggests that thyroid substance may have an effect on protein metabolism separate and apart from its effect on metabolism in general.

[1] Palmer, W. W., PROC. SOC. EXP. BIOL. AND MED., 1927, xxv, 229.

[2] Folin, O., *J. Biol. Chem.*, 1914, xvii, 469.