Isotopic Studies of the Body Potassium Content in Thyrotoxicosis.* (20723)

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Hyperthyroidism is characterized by an increase in the rate of all bodily functions. Among the more striking clinical features of the disease are generalized muscular weakness and loss of body weight. Degenerative changes in the skeletal muscle have been demonstrated by histologic technics. Creatine and nitrogen metabolism are altered. All of these observations indicate that there is some abnormality of muscle metabolism in this disease. Since muscle tissue contains the largest body store of potassium, a disturbance in potassium metabolism might also be suspected in the hyperthyroid state.

Because of the technical difficulties involved in the measurement of soluble cations, very few data concerning the metabolism of potassium in hyperthyroidism are available. The introduction of flame spectrophotometry and the availability of synthetic radioactive isotopes have partially overcome these technical limitations. Direct measurement of the body store of potassium in intact animals is now possible by the use of a radioactive isotope of the atom-K^{42}(1). The ranges of values for the "total exchangeable potassium content (Ke)" in normal young men(1) and women(2,3), and also in various disease states(4), have been previously reported. The purpose of the present study was to determine the exchangeable potassium content in subjects with untreated hyperthyroidism.

Material. Subjects. Thirteen hospitalized subjects—6 males and 7 females—with the diagnosis of hyperthyroidism were studied; their ages ranged from 21 to 68 years. All subjects showed unequivocal clinical symptoms and signs of increased thyroid activity at the time of study. The clinical impression was confirmed in 12 instances by the finding of a basal metabolic rate of +25% or greater, or by a protein bound iodine determination showing a level higher than 10 μg per 100 cc of serum (Table I). In the 13th subject (Case 2), the serum cholesterol concentration was 188 mg per 100 cc. *Isotopes. Isotopic* potassium (K^{42}) was prepared for injection in the manner described by Corsa and his coworkers(1). The subjects were given 100 μc of K^{42} contained in 1.5 or 3 milliequivalents of potassium chloride solution, depending on the age of the solution.

Exchangeable potassium content (Ke). The determination of the exchangeable potassium content (Ke) was performed as soon as possible after the subject's admission to the hospital and prior to the initiation of therapy. Each subject received an intravenous injection of radioactive potassium by calibrated syringe between 7:30 and 9 a.m. The patient was then asked to void and to discard this specimen; all urine voided thereafter until 7 a.m. the following day was collected, and the K^{42} content of the pooled specimen was determined. Determinations of the specific activity were made on 2 spot samples of urine obtained at 8 and 9 a.m. on the day after injection. The following formula was used to calculate the value for the exchangeable potassium content of the body:

$$Ke = \frac{Ki^{42} - Ko^{42}}{Ku^{42}/Ku^{39}}.$$

Ke = quantity of exchangeable potassium in milliequivalents.

Ki^{42} = quantity of radiopotassium administered (arbitrary units).

Ko^{42} = quantity of radiopotassium excreted in pooled specimen of urine.

Ku^{42} = conc. of radiopotassium in spot samples.

Ku^{39} = conc. of nonisotopic potassium in spot samples.

Ku^{42}/Ku^{39} = mean specific activity of the 2 spot samples.

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TABLE I. The Exchangeable Potassium Content in Thyrotoxicosis, 13 Subjects.

Sex	Age (yr)	Ke (meq)	Wt (kg)	Ke/wt (meq/kg)	BMR (%)	PBI (μg %)	Wt loss (kg in mo)
♂	48	1421	75.5	18.8		26.9	59.1 12
♂	68	1413	45.5	31.1			22.7 9
♂	39	1491	56.4	26.4	+76		13.6 12
♂	27	1534	70.5	21.8	+98		13.6 3
♂	68	1660	60.0	27.7	+43		Not known
♂	21	2344	61.1	38.4	+25		None 12
♀	54	981	45.8	21.4	+36		13.6 24
♀	58	1556	59.1	26.3		16.8	Not known
♀	21	1895	55.5	34.1	+77		7.7 6
♀	54	1513	42.0	36.0	+40	11.2	13.6 8
♀	23	1369	46.4	29.5	+100		4.0 1
♀	50	1909	62.3	30.6		10.7	6.8 1
♀	59	1471	41.8	35.2	+41		65.0 24

Preliminary studies confirmed the observation of Corsa and his associates(1) that the specific activity of K^{42} in the urine reaches an equilibrium, in diseased as well as in normal subjects, within 24 hours(4).

Measurement of radioactivity. The activity of the urine and serum specimens was determined with a dipping tube and a scaling circuit. A total of 10,240 counts was made on each sample. All counting rates were at least 10 times background, and were usually in the range of 500 to 3000 per minute. At these counting rates, no correction for coincidence loss was necessary. All determinations were corrected for decay. The total *potassium* concentration in the urine was determined by flame spectrophotometry, using the method of Mosher and his coworkers(5).

Results. The reported range for Ke in normal males is 2770 to 4470 meq. with a mean of 3402 meq., or 35.6 to 53.6 meq/kg with a mean of 46.3 meq/kg(1). For normal females the range in one series(2) was 1374 to 2164 meq. with a mean of 1776 meq., or 25.1 to 37.9 meq/kg with a mean of 31.5 meq/kg; in another series(3), it was 28.0 to 47.2 meq/kg with a mean of 40.7 meq/kg.

Males. In the present study, all of the absolute Ke values in the males were below the normal range (Table I). When the Ke values were related to body weight, all but one were subnormal. The one normal value was found in a subject (Case 6) who had no history of weight loss. The individual (Case 1) who had lost the greatest amount of weight had the lowest value for Ke/wt. In general, therefore, there was a fair correlation between the Ke and the decrease in body weight.

Females. In the females the relation between weight loss, clinical symptoms and the Ke values was not as obvious as in the males. Of the 7 subjects, only one (Case 7) had subnormal values for Ke and Ke/wt (Table I). Although 5 of the remaining 6 gave histories of weight loss, the Ke values were within the normal range. One of these subjects (Case 13) had lost more weight than any other patient studied.

Comment. The results which were obtained in the male patients in the present study are compatible with the following interpretation: While abnormal production of the thyroid hormone increases the rate of catabolism of all body tissues, muscle tissue is most rapidly broken down. Consequently the decrease in body weight which occurs in this disease is due largely to a reduction in the body's muscle mass. As the muscle mass is reduced, the total exchangeable potassium content is decreased. Since this decrease in Ke is due primarly to a reduction in muscle mass, it does not necessarily indicate an intracellular metabolic deficiency (a decrease in the intracellular concentration of potassium). (In contrast, the metabolic abnormality which has been previously found, for example, in poorly controlled diabetes(6), apparently produces a true intracellular deficiency).

The variability of the results obtained in the females is more difficult to interpret, but can probably be explained on the basis of the differences in body composition normally

found between males and females. In health, the bodies of women contain proportionately more fat and less muscle tissue than those of men(7); the lower values for Ke/wt in normal females are attributed to this factor. When thyrotoxicosis occurs in women, fat is catabolized in preference to muscle tissue, so that the relative fat content decreases; hence, the Ke/wt value initially would tend to remain unchanged or actually to increase. With more severe or protracted thyrotoxicosis, which exhausts the store of fat, a proportionately greater quantity of muscle tissue is eventually catabolized and the Ke/wt value decreases to subnormal levels. Such may have been the case in subject 7.

The results of the present study suggest that the alterations in the exchangeable potassium content noted in thyrotoxicosis can be adequately explained on the basis of the nonspecific catabolic effects of increased thyroid activity. There is no evidence in the present study to suggest a defect in the intracellular metabolism of potassium.

Summary. 1. A radioactive isotope of potassium (K^{42}) was used to determine the exchangeable potassium content (Ke) in 13 subjects with untreated thyrotoxicosis. The Ke values were lower in untreated thyrotoxic males than in normal male subjects. It is concluded that the low Ke values could be attributed to a decrease in the total muscle mass of the body, resulting from increased catabolism of body tissue. 2. In contrast to the results found in men, the values for Ke/wt in untreated women were normal, with one exception. This sex difference has been attributed to the dissimilarity in body composition normally found between males and females. It is postulated that in women mild or early thyrotoxicosis decreases the relative fat content of the body. Muscle tissue is extensively catabolized only after the store of fat has been depleted.

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Aging Changes in Nucleic Acid and Protein-Forming Systems of the Virgin Mouse Uterus.* (20724)

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Several investigators(1-3) have established that nucleic acid concentration is much higher in rapidly growing embryonic tissue than in the corresponding adult tissue. Schulz(4) attempted to follow such a change in the mouse liver with aging but was unable to detect any changes in the concentration of either ribonucleic acid (RNA) or desoxyribonucleic acid (DNA). He expressed his results in terms of concentration of the nucleic acids per mg tissue. Since the extreme chromosomal polyploidy of liver tissue makes the use of RNA/DNA ratios of little use in so far as using them as an estimate of relative RNA per cell, it is possible that any change, if it did occur at the

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