11049 P

Effect of Testosterone Propionate on Creatinuria.*

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Numerous reports have been presented concerning the effects of castration, administration of androgens and estrogens in pure form, implantation of gonads, and injections of gonad extracts or saline suspensions upon creatine and creatinine metabolism in the normal and castrate animal. That a possible gonad relationship exists to creatine metabolism was shown by Rose[1] when he demonstrated a persistent creatinuria in children up to about the age of puberty. At this time creatinuria disappears in boys, but continues to a lesser or cyclic degree in girls and women. Read,[2] McNeal,[3] Remen,[4] Bühler,[5] and Pizzolato and Beard,[6] and others have presented evidence that castration in humans and animals leads to a creatinuria. In contrast, Tun-Chee-Shen,[7, 8, 9] Kochakian and Murlin,[10] Sandberg, Perla, and Holly,[11] and others have not observed an induced creatinuria in men, dogs, or rats by castration.

Considerable difference of opinion exists concerning the effects of sex hormones upon creatine and creatinine excretion in conditions of hypogonad function or castration. Bühler,[12, 13] Kun and Peczenik,[14] Paschkis and Schwoner,[15] and Kenyon, *et al.*,[16] find that androgens decrease hypogonad creatinuria. On the other hand, Pizzolato and Beard[6] claim that not only does castration in rats produce a creatin-

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TABLE I.

		Normal rats		Castrated rats	
	Day	Body wt, g	Creatine excreted, mg/kg body wt	Body wt, g	Creatine excreted, mg/kg body wt
Control period	2	563	0.9	488	1.2
	4	563	1.0	488	0.0
	6	563	0.5	488	0.0
	8	563	0.0	488	1.4
Fed creatine 40 mg/kg body wt	16	563	8.7	488	9.0
	18	557	12.0	488	12.0
	20	557	15.7	490	15.0
	22	557	11.0	490	14.7
	24	557	13.0	490	16.7
	26	557	15.5	490	20.0
	28	557	21.0	490	22.0
Fed creatine and injected testosterone propionate	30	557	20.7	490	21.2
	32	560	20.2	492	19.7
	34	566	20.0	512	18.0
	36	574	13.0	520	6.5
	38	588	13.7	538	2.7
	40	588	15.0	554	6.5
	42	588	18.7	548	15.0
Discontinued creatine and androgen	44	586	20.0	548	12.5
	48	578	11.0	544	1.0
	52	574	5.7	541	1.2
	56	568	0.5	538	1.5

uria but that testosterone propionate administration also increases it.

In view of the many conflicting reports and the realization of the difficulties attending the determination of creatine and creatinine, it was decided to study the quantitative determination of creatinine by means of the Jaffé reaction using the Evelyn photoelectric colorimeter and the Miller-Dubos specific enzyme for destroying creatine and creatinine. This was then applied to the study of the effect of testosterone propionate on exogenous creatine excretion in the normal and castrated adult male albino rat.

Sixteen male rats, all of the same age, were used. Eight of these were castrated at 3 months of age. All were placed in pairs in metabolism cages and kept in a constant temperature room which was maintained at 22°C. The urinary creatine investigations were divided into 4 periods: (1) a control period, (2) oral administration of creatine daily, (3) oral administration of creatine plus injection of 900 gamma of testosterone propionate daily, and (4) a period in which creatine and androgen were discontinued. The body weight and urinary creatine values of normal and castrated rats during these periods are shown in Table I.

These values for normal and castrated rats show the following: (1) the creatinuria in the control period is of a very low order; (2) as creatine is administered orally an intense creatinuria ensues; (3) as testosterone propionate and creatine are administered, there is produced a decrease in creatinuria, and a simultaneous increase in body weight which approximates a new high level. After this level is reached, creatine begins to appear again in greater quantities in the urine; and (4) in the fourth period where creatine and androgen were discontinued, there occurs a slight decrease in body weight and a return of creatine excretion to the pretreatment values. Therefore, the normal and castrate rats react in a similar fashion, but the changes in creatinuria and body weight are much greater in the castrate than in the normal animal.

The estimation of the creatine content of the gastrocnemius muscle in these rats with and without androgen administration, but always with a liberal supply of exogenous creatine showed no significant differences between the normal and castrated animals.

The gain in body weight of the animals is in accordance with the observations of many workers. Korenchevsky, Dennison, and Brovain[17] observed that the lower weight of castrated rats was elevated by injections of testosterone. Kenyon, Sandiford, Bryan, Knowlton, and Koch[18] have shown a definite weight increase in their eunuchoids during testosterone propionate administration. They feel that one-seventh to one-half of this gain may be due to protein being laid down as indicated by the nitrogen retention studies. They believe that a considerable amount of the weight increase is due to water and sodium retention. Similarly, Thorn and Harrop[19] have found that sodium and its associated water is retained in the normal dog during administration of estrone, estradiol, progesterone, pregnandiol, and testosterone, thus producing an increase in body weight.

Since it is generally believed that creatine when ingested is in part stored by the muscles, and that approximately 98% of the body's creatine resides in the musculature, it seems possible that the increased creatine retention, observed in the experiments described, paralleling body-weight gain, indicates increased muscle-tissue production under the influence of testosterone. This view is supported by the observation of Papanicolaou and Falk[20] who showed that the temporal muscles of male guinea pigs are larger than those of the females.

17 Korenchevsky, V., Dennison, M., and Brovain, I., *Biochem. J.*, 1936, **30**, 558.

18 Kenyon, A. T., Sandiford, I., Bryan, A. H., Knowlton, K., and Koch, F. C., *Endocrinology*, 1938, **23**, 135.

19 Thorn, G. W., and Harrop, G. H., *Science*, 1937, **86**, 40.

20 Papanicolaou, G. N., and Falk, E. A., *Science*, 1938, **87**, 238.

They also observed that in male and female castrates a muscular hypertrophy was produced by administration of testosterone.

It is, therefore, concluded that castration of adult male rats does not alter creatine excretion, that normal and castrated rats react in a similar fashion to exogenous creatine and testosterone propionate as far as creatine excretion and body weight changes are concerned, and that ingested creatine produces an intense creatinuria which is greatly inhibited by testosterone propionate administration.

11050

Changes in Excretion of Radioactive Na, K and in Carbohydrate Stores Twenty-four Hours following Adrenalectomy.*†

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Serious disturbances in electrolyte excretion and in carbohydrate storage have been observed in adrenal insufficiency. This investigation was undertaken with the hope of determining which of these two mechanisms first showed definite impairment. The findings presented here show that both conditions are altered in the rat 24 hours after the adrenals have been removed.

The altered rates of urinary excretion of radioactive sodium and potassium were interpreted as indicating altered excretion of these electrolytes. Evidence of alteration of carbohydrate metabolism was demonstrated by somewhat lowered values for blood sugar, and by lowered values for liver and muscle glycogen after glucose feeding. Separate groups of rats but of the same sex and approximately the same age, were used for these two studies, since it was not practicable to investigate both conditions in the same set of animals.

In the electrolyte excretion studies, male rats 10 weeks of age with an average weight of 268 g were used. The standardization of conditions for this experiment has been described previously.[1]

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