

CLXXVIII. THE EFFECTS OF TESTOSTERONE AND TESTOSTERONE PROPIONATE ON ADULT MALE RATS (COMPARED WITH THOSE ON FEMALE RATS)

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(Received 1 July 1937)

THE effects on castrated rats of injections of testosterone and of testosterone propionate have been studied in our previous papers [Korenchevsky & Dennison, 1936; 1937; Korenchevsky *et al.* 1936; 1937]. In the present paper we have studied the effects of both these hormones on normal male rats and of testosterone on normal female rats.

The effect of testosterone on the body weight, the weight of the testes, seminal vesicles with prostate, epididymis, adrenals and pituitary and the development of the mammary glands has also been investigated in young male rats by Selye *et al.* [1937] and by McEuen *et al.* [1936; 1937]. In their last experiment [1937] a daily dose of 2 mg. was injected for 22 days. The authors found that there was no inhibition of the somatic growth or change in weight of the adrenals and pituitary, but that the weight of the testes decreased considerably, while the weight of the seminal vesicles and prostate increased. The mammary gland developed slightly.

In the present experiments we used large daily doses of the hormones (500–1500 γ) in order to overcome any possible antagonistic influence of another hormone or other hormones, which might be present in the organism.

Technique

The experiments were performed on 24 adult male and 5 female rats belonging to 7 litters which were on the average 102 (males) and 84 (females) days old when killed. Injections were made for 21 days twice a day, half the daily dose being used for each injection. The artificial hormones were kindly supplied by Messrs Ciba, Ltd., and were dissolved in sesame oil.

The general technique was the same as that used in our previous experiments.

The effect on males of testosterone propionate compared with that of testosterone

The results obtained are summarized in Table I. Organs in which no change in weight was observed are omitted from the table.

Sexual organs. As can be seen from Table I the development of the testes was slightly depressed by both hormones to approximately the same degree.

The effect on the secondary sexual organs, however, while considerable with testosterone propionate was very slight or absent with testosterone.

Table I. *The effect on normal male rats of testosterone and testosterone propionate*

Organ	I	Rats injected daily with				V
	Control rats	Testosterone propionate		Testosterone		
		500 γ	1500 γ	500 γ	1500 γ	
Testes (g.)	2.89	2.46	2.59	2.38	2.63	
Seminal vesicles (g.)	1.10	2.05	2.56	0.96	1.23	
Prostate (g.)	1.24	1.87	1.96	1.17	1.42	
Penis (mg.)	325	383	406	323	334	
Preputial glands (mg.)	145	218	258	169	193	
Thymus (mg.)	303	158	92	335	435	
Retroperitoneal fat (g.)	13.4	9.7	11.4	12.6	12.8	
Final body weight (g.)	360	324	356	333	365	
Gain in body weight (g.)	+44	+31	+28	+49	+61	
No. of rats in group	7	5	7	3	2	

Although the larger dose (1500 γ) was three times the smaller (500 γ), the difference in the degrees of hypertrophy obtained in the seminal vesicles, preputial glands and more particularly in the prostate and penis with the two doses of testosterone propionate was small.

Thymus. The same difference in the activities of these two hormones was seen in the effect on the thymus, the involution of which was much hastened by testosterone propionate but unaffected by testosterone, the weight of the thymus being even greater in the "testosterone" rats than in the control rats.

Other organs. Neither of these hormones had any definite effect on the weight of the adrenals, thyroids, hypophysis, liver, kidneys, spleen or heart, the weights of which therefore are not included in the table.

Retroperitoneal fat and body weight. As can be seen in Table I, there was a slight decrease in the amount of fat and in the gain in body weight only after testosterone propionate injections. In agreement with the Canadian workers no effect on the somatic growth, as judged by the body weight, was seen after the injection of testosterone.

Note on the histological changes of the male sexual organs

In spite of the changes in the weight of the sexual organs histological investigation did not show any definite abnormalities in the testes, seminal vesicles and coagulating glands. Spermatogenesis was normal. Exceptionally, swelling and twisting of the heads of the spermatozoa (initial stage of degeneration) occurred in both the injected and uninjected rats.

The columnar epithelium of the ventral lobe of the prostate was often slightly higher in the rats injected with testosterone propionate than in the controls. Haematoxylinophil zones were generally definitely demarcated. The dropsical vacuolation of the epithelium of the ventral lobe was the only pathological feature seen and among 17 rats injected with both hormones only occurred in 3 rats which had been injected with testosterone propionate, in which rats it was of slight, or, in one rat, moderate development.

Taking into consideration that for a rat the doses used were exceedingly large, this slight abnormality does not contradict the general conclusion that testosterone and testosterone propionate even in such doses do not produce harmful effects on the sexual organs of normal male rats.

A comparison of the effects of the hormones on male and female rats

In the previous paper [Korenchevsky, Dennison & Hall, 1937] it was shown that the large dose of testosterone propionate (1500 γ) produced in female rats a "gigantic" uterus and vagina. In order to compare this effect with that of

Table II. *The effect on normal female rats of testosterone compared with that of testosterone propionate*

Organ	1	2		3
	Control rats	Rats injected daily with 1500 γ of		Testosterone propionate
		Testosterone		
Uterus (horn + cervix) (mg.)	376	426		955
Cervix (mg.)	112	159		359
Vagina (mg.)	226	339		550
Female preputial glands (mg.)	104	202		256
Thymus (mg.)	397	288		62
Body weight (g.)	222	206		227

testosterone, 5 normal female rats were used for the experiment: 2 were left as controls and 3 were injected with a daily dose of 1500 γ of testosterone for 20 days. These results are given in cols. 1 and 2 of Table II, only definite and constant data being included. Col. 3 gives the relative data from Table I of our previous paper [Korenchevsky, Dennison & Hall, 1937] with a similar dose of testosterone propionate. Since these rats were 98 days old, their proper controls are to be found in Table I of this previous paper. The data in Table II show that, although the effects of testosterone were much less than those of testosterone propionate, they are comparatively greater on the organs of female rats than on those of male rats. A definite hypertrophy of the secondary sexual organs and an increase in the rate of involution of the thymus were obtained in female rats after testosterone injections. Histologically, however, medium progestational changes were found only in the vagina (mucification of the epithelium). In 2 rats the uterus was similar to the usual dioestrous type, while in one rat a slight folding of the mucosa was present. The striking hypertrophy of the cells of the mucosa and myometrium seen in the "testosterone propionate" uterus was absent from the "testosterone" uterus. The injection of testosterone into female rats brought about no changes in the other organs examined, in the deposition of fat or in the gain in body weight.

SUMMARY

1. Experiments were performed on 24 normal male rats and 5 normal female rats and the results compared with those previously obtained.
2. *In male rats*, testosterone propionate brought about considerable hypertrophy of the secondary sexual organs and hastened the involution of the thymus, while testosterone had little or no effect on these organs. Both hormones slightly depressed the development of the testes to about the same degree.
3. Histologically the hormones, even in the extremely large doses used, showed no harmful effects on the sexual organs.
4. With testosterone propionate the deposition of fat and the body weight were slightly decreased.
5. *In female rats* the effects of testosterone on the development of secondary sexual organs and on the thymus were definite, but much less than those of testosterone propionate.
6. Histologically, after the injection of testosterone, progestational changes were found in the vagina but not in the uterus.
7. *In normal rats* both hormones caused a greater degree of hypertrophy of the female sexual organs than of the male sexual organs.
8. This fact particularly clearly demonstrates in normal rats the bisexual property of these hormones, which we had previously shown on gonadectomized animals.

Grants from the Medical Research Council and from the Lister Institute have enabled us to carry out this work and to them our thanks are due. We wish to express our gratitude to Messrs Ciba, Ltd., in particular to Dr K. Miescher, for the supply of testosterone and testosterone propionate.

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