

THE EFFECT OF TESTOSTERONE PROPIONATE ON THE SEX-LIFE OF THE FEMALE RAT

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THE action of hormonal substances on the smaller experimental animals is usually assessed by killing the animal and examining its organs shortly after treatment. The present paper deals with a study of the effects of testosterone propionate injections on the subsequent life of the female rat.

An earlier paper (Groome, 1939, which see for references) describes the immediate anatomical effects of testosterone propionate on the young female rat. In this instance the experiment was repeated, but instead of killing the females, when the course of injections was completed, males were introduced and the sexual cycle observed.

MATERIALS AND METHODS

Eight female rats 55 days of age and four of 74 days were divided into two groups. One group was kept for control purposes, while the six animals in the other group received subcutaneous injections of 500 γ testosterone propionate daily for 8 days. On the 9th day, when the animals were 64 and 83 days of age, adult males were introduced into the cages. Vaginal smears were taken until pregnancy, or until the cycle of pseudopregnancies, had been established. The young of the experimental animals were killed and examined; but the young of the controls were kept to replenish breeding stock, and as a result two small litters were unfortunately eaten by their parent before their sex had been noted. The twelve females with which the experiment started were all killed 60 days after the original introduction of the males, which will subsequently be called the 1st day of the experiment.

RESULTS

Oestrus was observed in the controls from the 1st to 4th day, and in each case fertile matings were made. The young were born between the 23rd and 26th day, the known sex ratio being 100 : 100. Some of the young and all the controls were killed on the 60th day and were found to be normal. The controls, weighed to the nearest 5 g., had an average body weight of 179 g.

Oestrus was much delayed in the experimental animals. The first oestrus of nos. 3, 4 and 6 was not observed from vaginal smears, but deduced from the presence of sperms in the vagina. In nos. 1 and 5 oestrus was delayed by 16 and

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12 days respectively, when fertile matings were obtained. No. 2 became oestrous on the 8th day, when a sterile mating delayed the next oestrus till the 22nd day on which a fertile mating occurred. No. 3 experienced two pseudopregnancies between the 7th and 34th day when she conceived. Nos. 4 and 6 had a sequence of pseudopregnancies, from the 9th and 7th day respectively, until they were killed on the 60th day. The vaginal smears of all these animals at first contained mucus only, then mucus and leucocytes and eventually, as the mucus disappeared, the typical pro-oestrous picture was obtained. A number of attempted copulations were noted when the vagina was in the mucous condition.

Table I. *Experimental animals*

	Days of age when male introduced	Oestrus observed days	Young born days	Young males	Young females	Wt. at death 60 days (g.)
1	64	16	39	1	0	155
2	64	8.22	44	7	4	170
3	64	7.(20).34	56	4	3	185
4	64	9.23 <i>et seq.</i>	—	0	0	185
5	83	12	34	2	3	195
6	83	7.21 <i>et seq.</i>	—	0	0	210
Controls						
1	64	3	25	3	3	170
2	64	3	25	3	3	170
3	64	2	24	3	2	185
4	64	3	25		3?	170
5	83	4	26		2?	195
6	83	1	23	2	2	185
2nd litter	—	—	57	3	4	

Columns 2, 3 and 6 refer to the number of days after the introduction of males.

The young were born between the 34th and 56th day, the sex ratio being 140 : 100; it will be seen from Table I that this ratio depends upon the abnormal litters of nos. 1 and 2. All the young were dissected and found to be normal, there being no tendency to intersexuality. The experimental females, killed on the 60th day and weighed to the nearest 5 g., had an average body weight of 183 g.

All the experimental females had hypertrophied and abnormally vascular clitoris-like organs, which were made prominent by the enlarged female preputial glands. The enlargement of the mammary apparatus was consistent with previous pregnancies or pseudopregnancies. The vaginae were normal to the cyclic condition of each individual. The uteri were indistinguishable from those of the controls, with the exception of nos. 4 and 6. The uteri of nos. 4 and 6 had the plicated appearance, typical of testosterone propionate activation, with reduced epithelial and glandular cells, but showing considerable thickening of the muscle and mucosa. The ovaries of all these animals were apparently normal and contained Graafian follicles and corpora lutea.

DISCUSSION

The course of testosterone propionate injections given to young female rats was the same as that described in an earlier paper; the immediate effects of the injections (Groome, 1939) can therefore be compared with their action over a period of 60 days.

The injections cause an immediate increase in body weight, but this is not maintained after 2 months.

The ovaries are activated by testosterone propionate, but after pseudopregnancies or pregnancy they are indistinguishable from normal.

In the earlier paper hypertrophy of the uterus with a progestational appearance, which might be genuine pseudopregnancy, is reported. In this experiment the cycle of pseudopregnancies was retained in the presence of the male until terminated by pregnancy. It will be noted that in the two animals which failed to become pregnant, the typical progestational type of uterus was retained for 60 days.

The injections caused vaginal mucification, which disappeared within 6 days in all cases.

The mammary glands are apparently unaffected, but the preputial glands and clitoris-like organ remain enlarged for 60 days. It appears therefore that the ovary will maintain the hypertrophied preputial gland; and that the clitoris-like organ will maintain its increased length long after the injection of androgens has ceased.

Testosterone propionate will delay oestrus by from 6 to 12 days, and pregnancy is delayed by from between 11 and 30 days to 60+ days. The sex ratio of the young born to treated females was abnormally high, but as this figure depends on one large litter only it has no significance.

It is of course impossible to be certain that each individual receives the same dose by injection, but it seems probable that there is considerable variation in individual sensitivity to testosterone propionate. It may be recalled that in the earlier experiment the injections caused "hypertrophy of the uterus, in one case having an oestrous, and in the others a progestational appearance". The individual differences here recorded are however differences of intensity rather than of fact.

From the point of view of the time factor the clitoris-like organ and preputial glands are most affected by testosterone propionate; the uterus is intermediate, and the vagina is least affected by it. The effect on the ovaries is more difficult to determine. It was suggested in the earlier work that they were activated by testosterone propionate, but that their effect on the principal accessory organs was masked by the direct action of the injection. The normal cyclic changes of the ovary are evidently not disorganized for long, as shown by the recurrent oestrus and pseudopregnancy. The failure to conceive was probably due to the condition of the uterus alone. On the other hand, the apparent willingness of both sexes to attempt copulation, when the vagina was anoestrous and contained mucus, may indicate that the normal ovarian cycle was not impaired; for there is no reason to suppose that the mere cornification of the vagina provides the stimulus to copulate

for either sex. It can, however, be stated that the injections temporarily remove the control of cyclical changes in the uterus and vagina from the ovary, which may itself retain an undisturbed cycle.

SUMMARY

Males were introduced into the cages of six young female rats, which had been injected with 500 γ testosterone propionate daily for 8 days.

Oestrus was delayed by from 6 to 12 days and was followed by recurrent pseudopregnancies or pregnancy. The young were sexually normal and sex-ratio was not significantly affected.

The injections caused vaginal mucification, which disappeared within 6 days.

These animals (and six controls) were killed on the 60th day when it was found that:

(1) There was no abnormal increase in body weight or in the mammary glands. The ovaries appeared normal.

(2) There was hypertrophy of the preputial glands and clitoris-like organ.

(3) The uteri of two animals that had been recurrently pseudopregnant, but not pregnant, had the typical plicated progestational appearance of testosterone propionate activation.

It is suggested that the delay in conception in all cases was due to the condition of the uterus, which underwent a cycle of pseudopregnancies (possibly initiated by the injections) in the presence of the male, until this cycle was terminated by pregnancy.

It is also suggested that the treatment temporarily removes the control of cyclical changes in the accessory organs from the ovary, which may itself retain an undisturbed cycle.

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REFERENCE

GROOME, J. R. (1939). *Quart. J. exp. Physiol.* **29**, 367.