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Effects of Testosterone Propionate in Spayed Female Rats.*

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It has been shown[1, 2, 3] that there are well defined differences in the response of female rats to testosterone propionate depending upon the time of the first injection in relation to estrus and diestrus. Since these differences seem to depend on the presence of persisting active corpora lutea in the animals first treated at estrus,[2, 3] the purpose of this study was to determine the effect of castration in order to remove all ovarian factors.

A total of 36 female rats from the Stanford colony was studied. They were divided into 6 groups, each consisting of 6 animals (Table I). They were 107 ± 5 days of age. Their estrous cycles were studied by vaginal smears for 29 days prior to the experiment. Six animals were castrated during estrus, the first injection of testosterone being given at that time. The second group was castrated at the second day of diestrus and testosterone injection was begun at that time. Testosterone propionate suspended in oil was administered subcutaneously in doses of 0.4 cc (4 mg) every second day over a period of 20 days totalling 4 cc or 40 mg. The remaining 4 groups were used as controls. Two were treated exactly as the above except that 0.4 cc of sesame oil was given every second day instead of testosterone. The last 2 groups were given oil only but were not castrated. In all instances the animals were killed 24 hours after the last injection of either testosterone or sesame oil.

The effects of the above treatments are recorded on the accompanying table (Table I). There was a slight difference in the gain of body weights of the rats receiving testosterone, but probably not to a significant degree so that castration apparently inhibited the increase in body weight which has been noted in normal animals.[3] The injection of the male hormone prevented castration atrophy of the

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1 Wolfe, J. M., and Hamilton, J. B., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 189.

2 Laqueur, G. L., and Fluhmann, C. F., *Endocrinology*, 1942, **30**, 93.

3 Schilling, W., and Laqueur, G. L., submitted for publication.

TABLE I.
Organ Weight Changes in Grams in Spayed Female Rats After Injections of Testosterone Propionate.

Groups	No. of rats	Material injected	cc inj.	Time 1st inj.	Increase body wt	Uter.	Ovar.	Adr.	Thyr.	Liver	Kidn.
Castrates	6	T*	4	E	5.16	.399	—	.035	.014	10.30	1.99
"	6	S†	4	E	4.00	.088	—	.046	.014	10.05	1.78
Normals	6	S	4	E	3.50	.415	.056	.059	.015	8.35	1.41
Castrates	6	T	4	D	4.50	.402	—	.034	.013	9.96	1.97
"	6	S	4	D	3.33	.098	—	.051	.014	10.17	1.82
Normals	6	S	4	D	4.00	.354	.049	.044	.013	8.61	1.51

*T = Testosterone. E = Estrus.
†S = Sesame Oil. D = Diestrus.

uterus regardless whether injected at diestrus or estrus. In all 6 groups no significant difference was observed in the average weights of the thyroid gland and liver while an increase in the weights of the kidneys and a decrease in the weights of the adrenals were observed in the animals given the hormone. The decrease in adrenal weight, however, was directly comparable to the change observed in non-castrates receiving the first injection of testosterone during diestrus.[3]

In castrates treated with testosterone no difference was noted in the histologic appearance of the uteri, mammary glands, and vaginae regardless of the time of the first injection in relation to estrus or diestrus. The morphology of these tissues was exactly the same as that occurring in normal non-castrated females given testosterone at late diestrus.[2] The vaginal epithelium was in a state of mucification, the uterus enlarged and the endometrium proliferated into lace-like folds. The mammary glands exhibited an increase of intertubular fibrous tissue, overgrowth of the ducts, some evidence of secretion but no proliferation of the acini. These findings are distinctly different from those obtained with normal rats receiving the first injection of testosterone at estrus which induces a hypertrophy of corpora lutea.[2]

Summary. In sexually intact female rats genital tissues react differently to testosterone propionate depending upon the time of first injection in relation to estrus and diestrus. In castrates no such difference is apparent. Here the reaction of the genital tissues is the same as those observed when testosterone is first administered at late diestrus to non-castrates.