

## Masculinization of Female Rats by Postnatal Administration of Male Sex Hormone.

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The production of intersexuality in rats has been reported.<sup>1, 2</sup> These animals were obtained by injecting the pregnant mother with male sex hormone during pregnancy. Only the genetically female offspring were affected. Well affected animals had a penis instead of a clitoris and no external or lower vagina. These animals also had prostates and seminal vesicles. Dantchakoff has also obtained similar changes in the embryonic guinea pig by injection of testosterone propionate directly into the amniotic cavity. Growth and modification of the clitoris in castrated females into which testes have been transplanted has been reported.<sup>3</sup> During the progress of this work Lacassagne and Raynaud<sup>4</sup> have reported the production of a penis-like organ in female mice injected continuously from birth to 6 weeks with testosterone propionate.

The embryological development of rats is relatively slow and the offspring are born in an almost fetal state. In the female new-born for example, the lower vagina is represented by a solid cord of epithelium that caudally merges with the posterior epithelium of the urethra which empties at the primary urogenital ostium. The clitorine urethra (which is present in the normal adult female rat) is not completely formed until 48 to 72 hours postpartum.

It seemed possible that developmental changes could be produced by injecting the female new-born with male sex hormone. Accordingly new-born female rats were injected with small doses of testosterone (0.1 to 0.3 mg. per rat in a single dose) within 24 hours after birth. No changes were obtained in these animals. Another series of animals were then injected with very large doses (2.5 to 17.5 mg. per rat, total dosage) of testosterone propionate\* at 2- or 3-day intervals until the twenty-first day after birth. Nor-

<sup>1</sup> Greene, R. R., and Ivy, A. C., *Science*, 1937, **86**, 2226.

<sup>2</sup> Greene, R. R., Burrill, M. W., and Ivy, A. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 1.

<sup>3</sup> Lipschutz, A., *Arch. J. Entw. Mechan.*, 1918, **44**, 196.

<sup>4</sup> Lacassagne, A., and Raynaud, A., *Compt. Rend. Soc. de Biol.*, 1937, **125**, 351.

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mal control littermates and the treated animals were killed and autopsied after maturity. The findings are shown in Table I.

TABLE I.

Litter No.	No. Treated Females	No. Control Females	Total Dosage Given	Days Dosage Given	Phallus	Vagina
12	2	3	0.1T	1st	Normal	Normal
	1		0.2T	1st	" "	" "
13	1	1	0.3T	1st	" "	" "
14	3	3	0.3T	1st	" "	" "
17	1	2	0.3T	1st	" "	" "
53	2	2	2.5TP	21	Penis-like	Minute orifice base of phallus
40	3	2	10.5TP	21	" "	Urethra and vagina had common opening at base of glans
37	2	2	12.0TP	21	" "	No vaginal orifice
36	3	3	12.0TP	21	" "	" " "
30	3	0	17.5TP	21	" "	" " "

The control animals were normal in all respects. The injected animals receiving the large doses had masculinized external genitalia, inasmuch as the phallus resembled a penis and the development of the external vagina was inhibited. It is to be noted that with the highest dosages (12-17.5 mg. of testosterone propionate) the vagina ended blindly under the perineal skin. With a dosage of 10.5 mg. the vagina and urethra had a common opening at the base of the phallus. These openings were not visible externally, but were covered by apparently normal preputial skin. With 2.5 mg. of testosterone propionate the vaginal orifice was present as a minute opening through the preputial skin at the caudal base of the phallus. The phallus in these affected animals resembled a normal penis insofar as the development of the corpora cavernosa was concerned, but the corpus spongiosum urethræ was not as well developed and the phallus was bent caudally. An *os priapi*, which is present in the normal male rat, was found in the affected animals. A right ventral lobe of the prostate (para-urethral gland) was observed under a dissecting microscope in 3 of the affected animals.

*Conclusion.* The administration of a sufficient quantity of testosterone propionate to the new-born female rat will cause a masculinization of the external genitalia.