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SECTION MEETINGS

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Further Effects of Androgenic Substance on Sexual Development in the Female White Rat.

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The production of intersexed rats by administration of testosterone to the pregnant mother of these animals has been reported.[1]

One hundred and fifty-two female albino rats have been injected with varying amounts of testosterone and testosterone propionate*

[1] Greene, R. R., and Ivy, A. C., *Science*, 1937, **86**, 200.

* We wish to thank Dr. Schwenk of Schering Corporation for the generous supply of testosterone and testosterone propionate used in this work.

at different periods of pregnancy. The testosterone has been given by multiple subcutaneous injections, the testosterone propionate by both single and multiple injections. The pregnancy of 97 of these rats has terminated by resorption or by delivery of necrotic fetuses. Fifty-five have delivered at term, spontaneously or by cesarean section. Females of 19 litters have survived to maturity and have been autopsied. In addition, females of 10 litters whose mothers have received high dosages are now living. Of the 19 litters autopsied, the females of 7 litters were normal. The mothers of these animals received apparently subthreshold dosages (1.65 to 3.5 mg. of plain testosterone and 0.5 to 2.5 mg. of testosterone propionate).

It was stated in our previous report that well affected adult animals had no distal vagina and that the blindly ending upper vagina and the uteri may become distended with retained secretions. This has been confirmed by Hamilton and Gardner.[2] In 8 adult intersexed animals since obtained whose mothers have received higher dosages (5.0-9.0 mg. testosterone propionate and 13.5 mg. plain testosterone), the uteri and upper vagina were not distended. Serial sections and wax reconstructions of 2 of these animals have revealed that the vagina communicates with the urethra by bilateral ostia medial to the ostia of the ejaculatory ducts. Identical conditions have been found in serial sections of 3 new-born whose mothers received similar dosages. This condition may be logically interpreted as a preservation of the original bilateral junctions of the mullerian ducts with the urogenital sinus. Serial sections of a new-born whose mother received smaller dosages (3.5 mg. testosterone propionate) reveal bilateral communication of the epithelium of the vagina with the urethra, but with this dosage the communication is represented by a non-patent solid cord of cells. The adult litter mate of this animal displayed the typical utero-vaginal distention associated with this condition.

In our previous communication it was stated that inhibition of mullerian duct derivatives had been obtained. This evidence has been limited, however, to 2 serially sectioned new-born. We have been unable to confirm these findings, since in 46 new-born and 21 adult intersexed animals examined to date, uteri and oviducts are present.

The presence in adult intersexes of structures that resembled seminal vesicles was reported. Such structures have been identified in 8 adult animals. A further development of wolffian duct deriva-

[2] Hamilton, J. B., and Gardner, W. A., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 570.

tives has been subsequently noted. Examination under a dissecting microscope of new-born animals whose mothers have received high dosages (5.0-14.0 mg. testosterone propionate and 13.5 mg. plain testosterone) has revealed a persistence of the vas deferens adjacent and parallel to the uterus. This structure was present on one side in 10 animals and on both sides in 15 animals. The wolffian duct derivatives are present from gonad to urethra as was demonstrated by serial sections, graphic and wax plate reconstructions. Efferent tubules connect with the rete of the gonad and continue into a well marked epididymis, vas deferens, and ejaculatory duct. Anlage of the seminal vesicles are present, but seem to be displaced cephalad so that the ejaculatory duct is relatively longer than the ejaculatory duct of a normal new-born male. In 3 experimental animals (mother given 6.0 mg. testosterone propionate) at an adult age, efferent tubules, head and tail of the epididymis, vas deferens, seminal vesicle, various prostatic lobes, Cowpers glands and a penis were present combined with apparently normal oviducts, uteri and upper vagina.

Study of the peni of these animals is as yet incomplete but an *os priapi* which is found in the normal adult male is present.

The gonads of adult animals whose mothers received low dosage of the hormone are grossly normal with visible corpora lutea. The gonads of animals prenatally affected by higher dosages are smaller and present a smooth white surface. Corpora lutea are not grossly visible and microscopic examination shows that they are absent. Follicles are present. An extensive rete is present and medullary tubules extending from the rete into the stroma of the gonad have been noted. A more detailed histological study of the gonads is in progress.

Summary. Sixty-seven intersexed rats, produced by injecting the pregnant rat with testosterone, have been examined. Testosterone given to the pregnant rat may in some instances arrest the fusion of the caudal portions of the mullerian ducts and the unfused portions are patent and open into the urethra. In addition, a number of animals have been produced in which wolffian duct derivatives, efferent tubules, epididymis, vas deferens and seminal vesicles are present in association with a fallopian tube, uterus and the upper portion of the vagina and with masculinization of the female gonad.