9273

Prostatic Type of Paraurethral Glands Induced in Female Rats by Administration of Male Sex Hormone.*

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On the basis of histologic[1] and embryologic[2] data the paraurethral glands (Skene's ducts) of women have long been considered homologous to the prostate of man, in particular to the cranial and ventral lobes.[3] In rats these glands have only recently been described[4] and studied embryologically.[5] It has later been reported that injection of the male sex hormone stimulates the growth and development of these glands in the female rat; in contrast they are not affected by oestrone.[6] In view of the scarcity of definite data on Skene's ducts and their relation to the formation of cysts[7] in women, it is deemed worthwhile to present the following confirmatory evidence of a homologous relation to the male prostate and their control by the male hormone. Further, the reaction of these glands to the male hormone alone (as far as is known) distinguishes them as a biologic indicator for the presence of the male hormone in the female.

A series of 64 mature and 32 immature female rats were divided into 4 groups which received as follows: (a) 500 γ of testosterone acetate* or testosterone propionate,* (b) 500 γ of oestrone,* (c) 500 γ of testosterone acetate and 500 γ of oestrone, (d) only the oil vehicle. Therefore, rats in groups (a) and (b) were given, respectively, equal amounts by weight of the male hormone, testosterone acetate, and the female hormone, ketohydroxyoestrin, whereas rats in group (c) were given both male and female substances. Both hormones were dissolved in the same quantity (3 mg./cc.) of the

* Aided by a fund provided by Doctor George Walker.

1 Virchow, R., *Arch. f. path. Anat.*, 1853, **5**, 403.

2 Tourneux, F., *Compt. rend. Soc. de biol.*, 1888, **40**, 81. Evatt, E., *J. Anat. and Physiol.*, 1910, **45**, 122. Sachs, O., *Wien. klin. Wchnschr.*, 1911, **24**, 1420. Johnson, F., *J. Urol.*, 1922, **8**, 13.

3 Pallin, G., *Arch. f. Anat. u. Entwickel.*, 1901, p. 135.

4 Marx, L., *Z. Zellforsch. u. mikr. Anat.*, 1932, **16**, 48.

5 Price, D., *Am. J. Anat.*, 1936, **60**, 79.

6 Korenchevsky, V., and Dennison, M., *J. Path. and Bact.*, 1936, **42**, 91; **43**, 345.

7 Sachs, O., *Wien. klin. Wchnschr.*, 1911, **24**, 1420.

* Testosterone acetate and testosterone propionate were furnished through the courtesy of the Ciba Company; oestrone (theelin) through the courtesy of Parke, Davis and Company.

same oil (peanut oil), since the amount and type of oil influences the absorption.[8] All injections were made subcutaneously. Some animals were sacrificed on the 11th day; in other animals the administration was continued for as long as 3 months.

Results. From embryological studies by Price[5] and from experimental stimulation by injections of male hormone by Korenchevsky and Dennison[6] and by the present authors it is apparent that the female prostatic glands are homologous to male prostatic glands and are located caudal to the bladder in an urethral position similar to that of the ventral portion of the prostate in the male animal. Grossly, the glands resemble the male prostate. They present a pale flesh-pink color, a stippled surface and contain a clear, watery secretion similar to that of the male prostate. The glands are in the form of 1 or 2 disc-like lobes, which may reach a weight of 70 mg. in a single animal. Either a bilobular or unilobular condition may be present, the latter being more common with the lobe lying on either the right or left side of the urethra. In the bilobular condition one lobe lies on each side of the urethra. No opening from the glands into the urethra has been seen in serial section of the glands and urethra, but more material must be studied before denial is made of an outlet of the glands.

Histologically, the gland is composed of prostatic-like alveoli which are distended with fluid and lined with either cuboidal or columnar epithelium. Near the periphery of the lobe the alveoli are relatively small; they are lined by a tall columnar epithelium which is in some instances thrown into folds. The epithelium on the apex of these invaginations is usually pseudostratified. Alveoli in the more central portion of the lobe are commonly more distended with secretion with lining cells of a cuboidal type. The cells lining the alveoli save those of the low cuboidal type present a light-staining area in the cytoplasm distal to the nucleus similar to that described in the prostate. The nuclei are light-staining, vesicular, and proximally placed. The interalveolar spaces contain a few smooth muscle fibers surrounding the individual alveoli and considerable connective tissue, which is relatively more abundant near the periphery of the lobe.

The incidence of glands visible to the eye was low (9.4%) in 35 untreated virgin females; the few glands found were in young animals. In spayed animals and in those receiving oestrone Skene's glands were not observed. In the 48 animals receiving male hormone, the incidence was 58.3% (Table I).

[8] Parkes, A. S., *Lancet*, 1936, **2**, 674.

TABLE I.
Summary Table of Macroscopic Observations on Incidence of Skene's Ducts in Control and in Hormone Injected Rats.

Treatment	Paraurethral Glands		% Present
	Absent	Present	
Testosterone acetate or propionate 500 gammas daily—10-39 days	15	23	60.5
Testosterone acetate and ketohydroxyoestrin 500 gammas of each	5	5	50.0
Ketohydroxyoestrin 500 gammas	13	0	0.0
Control	32	3	9.4

The incidence of the paraurethral glands may be much higher than indicated by the figures in Table I, for counts included only macroscopically visible lobes. In the absence of routine histologic study and in view of the limited number of animals, these percentage figures are tentative and will probably need revision.

Skene's ducts are not only the embryologic homologue of the male prostate, but as previously indicated, also respond to the male hormone; they are not stimulated by oestrone but in either spayed or normal animals develop after male hormone administration into structures grossly and histologically similar to the male prostate.[6] The growth of Skene's ducts in response to male substances is in agreement with studies[10, 11] demonstrating the masculinizing or androgenic influence of male hormones in the female, particularly on those organs (clitoris, preputial and paraurethral glands) whose counterparts in male animals respond vigorously to male hormone.

The embryologic similarity of these glands to the prostate and their development in animals injected with male hormone but not in those injected with female hormone are evidence of the dependence of these structures upon the male substance. It is suggested that Skene's ducts of the rat may be of use as an indicator in the female of the effect of injections of male substance.

The occasional finding of well-developed glands in a normal uninjected female may be interpreted tentatively as indicative of the presence of male hormone-like substance in normal female animal under certain conditions. Further evidence that a substance similar to the male hormone may be produced in normal females is shown by recent studies[12] in which injection of large amounts of A.P.L.

[9] Moore, C. R., Price, D., and Gallagher, T. F., *J. Anat.*, 1930, **45**, 71.

[10] Hamilton, J. B., *Anat. Rec.*, 1937, **67**, 22.

[11] Hamilton, J. B., unpublished data.

[12] Wolfe, J. M., *Anat. Rec.*, (in press).

into normal male or female rats, simultaneously with oestradiol resulted in a partial suppression of the reaction of the anterior lobe to oestradiol, a result which has since been duplicated by injecting male hormone simultaneously with oestrone.[13]

Summary. 1. Skene's ducts in the female rat are usually rudimentary. Male hormone substance stimulates growth of these glands to a condition which resembles grossly and histologically the prostate of the male rat. 2. In the present series the incidence of these glands in 35 normal animals is 9.4%, in 13 oestrone-injected animals 0%, in 48 male hormone-injected animals 58.3%. 3. The state of Skene's ducts may be utilized as an indicator of the presence of male hormone. 4. In view of the growth response to male but not to female hormones, the occasional finding of Skene's ducts in an uninjected female rat suggests the presence of male hormone in the normal female. 5. The growth response of the female prostatic glands to the male hormone is further evidence of the masculinizing effect of male hormone substance of the female animal.

9274

The Localized Sanarelli-Shwartzman Phenomenon in the Rabbit Kidney.

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A new phenomenon of tissue reactivity to bacterial filtrates has recently been described. The filtrates of many bacteria, hitherto not considered to produce exotoxins, have been shown to exert a marked toxic effect when 2 injections into a rabbit, the second injection being intravenous, are separated by an interval of 24 hours. The generalized reaction resulting when the first, or "preparatory" injection is given intravenously was described by Sanarelli,[1] and studied in detail by Apitz,[2] Gratia and Linz,[3] and Gerber.[4] The localized reaction resulting when the preparatory injection is given

[13] Wolfe, J. M., and Hamilton, J. B., *Anat. Rec.*, 1937, **67**, 55.

* Research Fellow in Medicine, Harvard University.

[1] Sanarelli, *Ann. de l'Inst. Pasteur*, 1924, **38**, 11.

[2] Apitz, K., *Virchow's Arch. f. path. Anat.*, 1934, **293**, 1.

[3] Gratia, A., and Linz, R., *Ann. de l'Inst. Past.*, 1932, **49**, 131.

[4] Gerber, I. E., *Arch. Path.*, 1936, **21**, 776.