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THE FEMALE PROSTATIC GLAND AND ITS REACTION TO MALE SEXUAL COMPOUNDS

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In previous papers [Korenchevsky, 1935; Korenchevsky & Dennison, 1936*a*] a historical review was made of the literature dealing with the female prostatic glands (minute in size and atrophic in structure) in human beings and a short description was given of our detection of this gland in the rat. In these papers, however, detailed histological examination of the female prostate was not made and photomicrographs were given only at low magnification ($\times 12$ or $\times 15$) at which magnification it is not possible to come to any conclusion as to the structure of the glandular cells either in the uninjected or the injected rats, or as to the homology of the female gland with the ventral lobe of the male prostate. In this paper we give this evidence. At the same time we give photographs of the glands hypertrophied by some of the male sexual compounds used in our latest experiments and which have not been described in our previous papers.

The nature of the experiments on the female rats, the prostatic glands of which are described in this paper, has been published elsewhere [Korenchevsky & Dennison, 1936*c*; Korenchevsky *et al.* 1935, 1937, 1937*a*, *b*].

Technique

The details of the general technique of the experiments are given in our previous papers, which have been mentioned above. Some of the data referring to the rats described in this paper are given in Table I. All the injected rats given in Table I (except in the case of one group which is mentioned) were spayed. The male sexual compounds used in all our experiments were artificially prepared and supplied by Messrs Ciba, Ltd.

TABLE I. Occurrence of the female prostate in female rats injected with male sexual compounds

Male sexual compound and daily dose	No. of rats in group	No. of rats with hypertrophied prostate	No. of rats with atrophic prostate (serial sections)
Androsterone, 0·9–3·6 mg.	27	0	0
Transdehydroandrosterone, 1–4 mg.	29	1	0
Androstane-diol, 0·49–3·54 mg.	37	5*	0
Testosterone, 0·167–0·7 mg.	26	1	0
Testosterone propionate (spayed rats), 0·167–0·7 mg.	18	1	0
Testosterone propionate (normal rats), 0·5–1·5 mg.	10	3	0
Δ^4-Androstene-dione, 0·5–3 mg.	27	2	0
Δ^5-Androstene-diol, 0·2–0·6 mg.	10	0	0
No compound injected	56*	0	9*
Total	240	13	9

Note. Figures marked with an asterisk are taken from a previous paper [Korenchevsky & Dennison, 1936*a*, p. 100]. Since œstrone does not prevent hypertrophy of prostate, the figures represent number of rats injected with male compound alone or simultaneously with œstrone (2–18γ per day, 3–7 times per week).

Only three (androsterone, transdehydroandrosterone and testosterone) of the seven compounds have so far been isolated from the organism, though the presence of the other is suspected. We therefore use the term "compound" rather than "hormone", this latter term usually being reserved for substances which are found in the organism.

The compounds were dissolved in sesame oil and injected in half daily doses twice a day. The daily doses injected are given in Table I, the period of injection being 21 days.

The organs were fixed in Bouin's fluid and embedded in paraffin. The sections were stained with hæmatoxylin and eosin and, when necessary, for fibrous and muscular tissue with Masson's trichromic stain.

Prostatotropic property of male sexual compounds in female rats

In our experiments on female rats (Table I) the following compounds brought about hypertrophy of the glands:

(1) transdehydroandrosterone,
(2) testosterone,
(3) testosterone propionate (an ester of testosterone),
(4) Δ^4-androstene-dione, and
(5) androstane-diol.

Negative results were obtained with androsterone and Δ^5-androstene-diol, which, however, does not mean that these hormones have no female prostatotropic property: the number of rats injected was too small for such a conclusion.

Normal occurrence of the female prostatic glands

The data summarized in Table I might be used in making a more correct (though certainly not final) determination of the normal occurrence of the female prostate in our stock of rats. The hypertrophied prostate is easily seen with the naked eye and cannot therefore be missed at dissection. With the exception of androsterone and androstene-diol all the compounds examined proved to be "female prostatotropic". Therefore, after the deduction of the 37 rats injected with androsterone and androstene-diol, all the rats injected with the other compounds may be included in the statistical calculation, i.e. 147 rats. To these the 56 control uninjected rats, in which serial section was made of the vagina [Korenchevsky & Dennison, 1936*a*], can be added. Thus, in 203 rats, in which a prostate was most unlikely to be undetected, it was found in 22 cases or in about 11 p.c.

Histology of the gland

Normal uninjected rats. In this group the largest prostate found is shown at low magnification in Pl. XXII, fig. 41, of our previous paper [Korenchevsky & Dennison, 1936*a*]. Pl. I, fig. 1, of the present paper shows the glands in one of the normal rats at high magnification ($\times 200$), while fig. 2 represents the gland in the other normal rat. Both rats were in diœstrus. Both glands show atrophic follicles, lined with cubical (fig. 1) or low columnar (fig. 2) epithelium, containing clear protoplasm, in which it is not possible to distinguish any separation into different zones. The greater the amount of secretion in the follicle the lower the cells. The development of the interfollicular interstitial tissue in relation to the follicular tissue is greater than in the females injected with prostatotropic compounds or in normal males. Fig. 2 shows a considerable increase in the fibrous tissue and also patches of small cellular (chiefly leucocytic) infiltration. Patches of this infiltration are often seen in the atrophic female prostates of the uninjected rats.

The structure of the gland in female rats during natural œstrus [Korenchevsky & Dennison, 1936*b*, Pl. LXV, fig. 19] and during pregnancy [Korenchevsky & Dennison, 1936*a*, Pl. XXII, fig. 42] was shown at low magnification in our previous papers. The histological structure at high magnification is the same as that shown in figs. 1 and 2 of the present paper. Such a structure is also typical of the male prostate atrophied after castration.

Spayed uninjected or œstrone injected rats. The histological structure is identical with that seen in the normal uninjected rats (figs. 1 and 2).

Transdehydroandrosterone injected spayed rats. Fig. 3 represents a gland found in a spayed rat injected with 1 mg. per day of transdehydroandrosterone simultaneously with œstrone. This male hormone is the weakest of the male hormones investigated by us [Korenchevsky & Dennison, 1936*c*], producing only a slight hypertrophy of the sexual organs in castrated male rats. The effect of this hormone on the female prostatic gland was also weak as is shown in fig. 3. The hypertrophy of the cells and follicles was only slight. There was no separation of the cell protoplasm into "clear" and "dark" zones. Therefore the chief effect of this hormone was to cause an increase to about double the size of the whole female prostate.

Spayed rats injected with androstene-dione, testosterone or testosterone propionate. The glands in the rats injected with these hormones were similar to those of the rats injected with androstane-diol [Korenchevsky & Dennison, 1936*a*, Pl. XXII, figs. 43 and 45]. As is shown in fig. 8 (present paper) the gland was considerably hypertrophied, appearing to the naked eye to be typical of the ventral lobe of male prostate. Fig. 10 shows at high magnification one of the small follicles situated at the periphery of the other gland. The less the amount of secretion in the lumen of the follicles, the less the cells are compressed and therefore the more fully are they able to develop. Thus, as is seen in fig. 10 and at still higher magnification in fig. 5, the epithelial cells are completely developed. The cells are columnar, nearly all the nuclei are situated at the basal part of the protoplasm. The protoplasm is quite definitely divided into three zones, two "dark" hæmatoxylinophil zones and between these a "clear" eosinophil zone. The larger "dark" zone occupies the basal half of the cell and a second much narrower zone faces the lumen of the follicle. The epithelial layer forms many villous projections into the lumen of the follicle. The blood vessels and a small amount of interstitial tissue is seen in the centre of the projections between the two epithelial layers.

Normal female rats injected with testosterone propionate. In normal injected rats the gland was hypertrophied to about the same size as that observed in spayed injected rats. Fig. 9 represents the largest of the prostates seen in this group. In order to economize space this gland is not shown at high magnification, since the only differences from the gland shown in fig. 10 that could be seen were an occasional vacuolation and, sometimes, a less marked distinction between the "dark" and "light" zones in the epithelial cells.

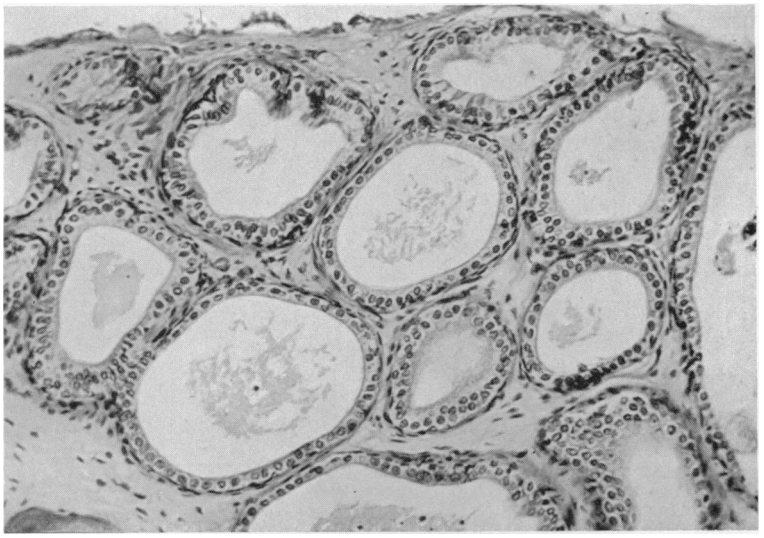

Fig. 1

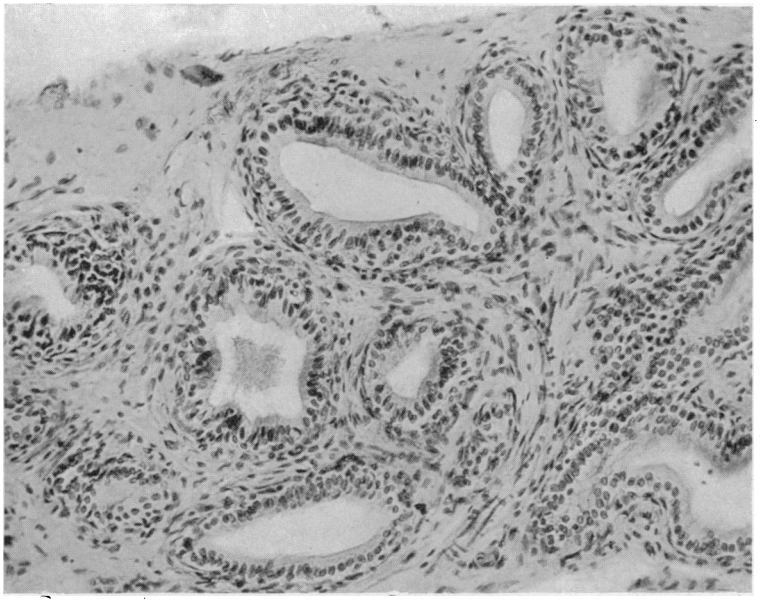

Fig. 2

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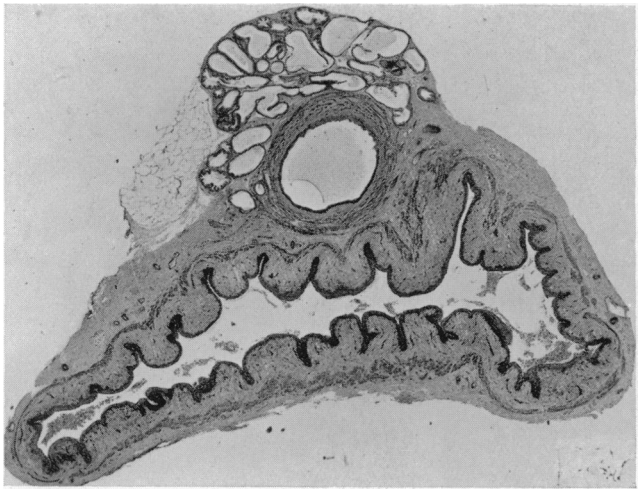

Fig. 3

Fig. 5

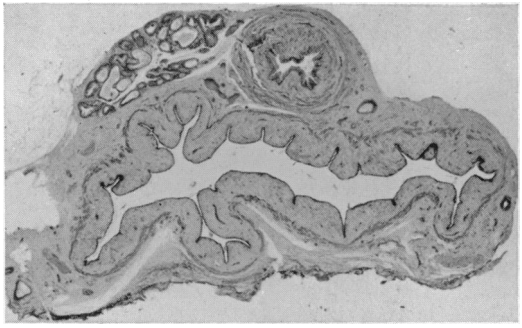

Fig. 4

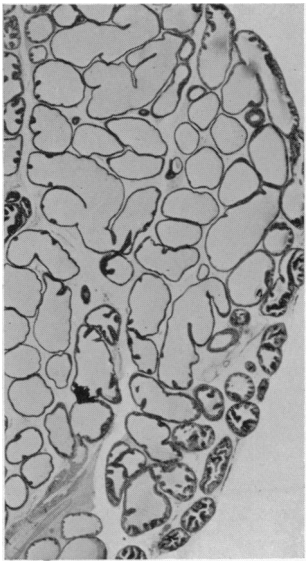

Fig. 6

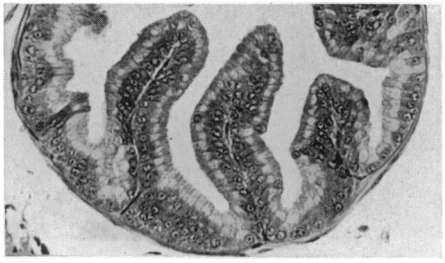

Fig. 7

Fig. 3

Fig. 9

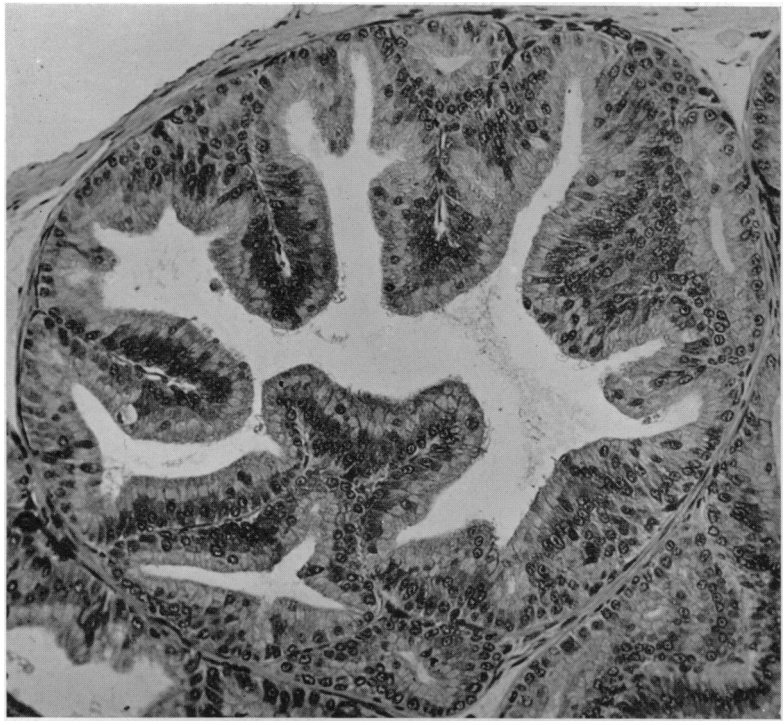

Fig. 10

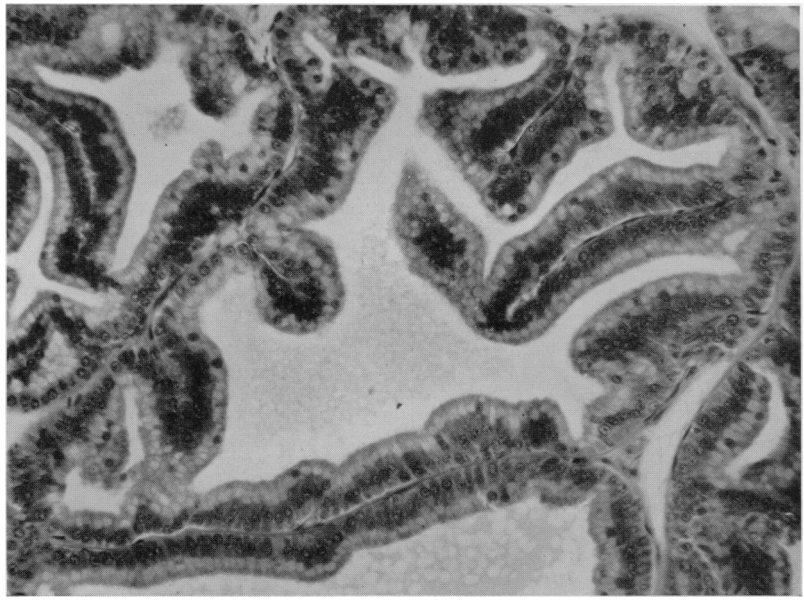

Fig. 11

A comparison of the female prostate with the ventral lobe of the male prostate. We have shown previously [Korenchevsky & Dennison, 1935, pp. 326–7), that in the male rat there are definite histological differences between the ventral, dorsal and lateral lobes of the prostate; nor can the ventral lobe be confused with any other gland in the organism. The three zones in the protoplasm, the form and arrangement of the cells in the follicles and the appearance and position of the nuclei are a unique combination characteristic only of the ventral lobe. When this is taken into consideration, there can be no doubt that the developed female prostate is histologically identical with the ventral lobe of the normal male prostate. Comparison of the photographs of the female prostates in figs. 3, 8, 9 (×15), fig. 10 (×200) and fig. 5 (×300) with those of the male ventral lobe in fig. 6 (×15) and figs. 7 and 11 (×200) show this clearly. The most important feature is the presence of the three zones in the cells. This proves that in the rat the female prostate is homologous with the ventral lobe of the male prostate.

The follicles and cells of the prostate shown in figs. 1 and 2 are identical in appearance with those of the ventral lobe of the atrophic prostate of the castrated male rat. In order to economize space, however, we do not give photographs of the latter, since it is not possible to differentiate the atrophic epithelial cells of the male and female prostate, not only from each other, but also from the epithelial cells of some other glands, since the atrophic cells do not show the three zones or other typical features of the male prostatic cells.

Summary

1. Development of the rudimentary prostatic glands into comparatively large female prostates has been obtained after the injection of five out of seven of the male sexual compounds examined.

2. The stimulation was weakest with transdehydroandrosterone and strongest with androstane-diol, androstene-dione and testosterone propionate.

3. A description is given of the detailed histological structure of both atrophic and hypertrophied female prostates.

4. The detailed histological comparison of the hypertrophied female prostate with the ventral lobe of the normal male prostate proves that these glands are homologous, and so confirms our previous conclusion.

Grants from the Medical Research Council and from the Lister Institute have enabled me to carry out this work, and to them my thanks are due. I am much indebted to Prof. A. Girard for the supply of œstrone, to Messrs Ciba, Ltd., for the supply of the male compounds and to Mrs M. Dennison, who prepared the photomicrographs.

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DESCRIPTION OF PLATES I–IV

PLATE I

Fig. 1. Rudimentary female prostate in a normal uninjected rat. Follicles and cubical epithelium atrophic. ×200.

Fig. 2. Rudimentary female prostate in a normal uninjected rat. Follicles and cylindrical epithelium atrophic. Greatly increased amount of fibrous tissue. ×200.

PLATE II

Fig. 3. Slightly hypertrophied female prostate in a spayed rat injected with 1 mg. trans-dehydroandrosterone per day + 6γ œstrone three times per week. Below, cross-section of vagina; above, round cross-section of urethra. Prostate above and on the left of urethra. ×15.

Fig. 4. Rudimentary female prostate in a spayed uninjected rat. Prostate, the largest in this group, on the left, between urethra and upper wall of vagina. ×15.

Fig. 5. Part of the villous projection of the female prostate shown in fig. 10 at ×300. Cylindrical epithelium showing three zones, with nucleus in basal dark zone. Structure of cells identical with those of male prostate shown in figs. 7 and 11.

Fig. 6. Part of ventral lobe of prostate of normal male rat. Similar to hypertrophied female prostates in figs. 3, 8 and 9. ×15.

Fig. 7. The same as in Fig. 6 but at magnification ×200. Small type of otherwise fully developed villous projections and cells.

PLATE III

Fig. 8. Greatly hypertrophied female prostate in a spayed rat injected with 3 mg. androstenedione per day. Prostate on the left, cross-section of vagina on the right and between these—urethra. ×15.

Fig. 9. Greatly hypertrophied female prostate in a normal rat injected with 1·5 mg. testosterone propionate per day. Vagina larger than normal, with completely mucified epithelium showing "pregnancy effect" of testosterone propionate. ×15.

PLATE IV

Fig. 10. Small follicle of greatly hypertrophied female prostate of a spayed rat injected with 167γ testosterone propionate per day. Fully developed villous projections and cells identical with those of normal male prostates shown in fig. 11. ×200.

Fig. 11. Small follicle of the ventral prostatic lobe of a normal male rat. Large type of fully developed villous projections and cells identical with those of female prostate in figs. 5 and 10, larger than those of male prostate in fig. 7.