

pig<sup>7, 8</sup> and also to the androgen produced by ovaries transplanted to the ears of untreated castrate mice<sup>9, 10</sup> and rats.<sup>11</sup> In a previous publication the present authors suggested that the androgen involved may be progesterone<sup>1</sup> since this substance has been shown to have androgenic potency in the rat.<sup>12, 13</sup> Experiments to test this hypothesis are in progress.

*Summary.* Ventral prostates from male littermates were implanted into female rats 10 days of age. Daily treatment with chorionic gonadotropin produced no evidence of androgenic stimulation in the prostates when the females were castrated. When the ovaries were not removed the prostates of the treated animals showed evidence of stimulation at 18 to 25 days, but not after 28 days of age.

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### Androgen Production in Normal Intact and Castrate Immature Female Rats.\*

M. W. BURRILL AND R. R. GREENE. (Introduced by A. C. Ivy.)

*From the Department of Physiology and Pharmacology, Northwestern University Medical School, Chicago.*

In the female white rat the homologue of the male ventral prostate is sometimes found. Witschi, Mahoney, and Riley<sup>1</sup> reported that in one strain of rats the incidence of female prostates was 8.8% and in another strain, of Wistar origin, it was 26.7%. They also found that, by selective breeding, the incidence of female prostates was increased to 77.3%. Price<sup>2</sup> has reported a low incidence (under 2%) for the rats of her colony. In our own colony, examination of 333 females has placed the incidence at 13.8%.

Contrary to the conditions in the male, the female prostate is not

<sup>7</sup> Papanicolaou, G., and Falk, E. A., *Proc. Soc. Exp. Biol. and Med.*, 1934, **21**, 750.

<sup>8</sup> Papanicolaou, G., and Falk, E. A., *Science*, 1938, **87**, 238.

<sup>9</sup> Hill, R. T., *Endocrin.*, 1937, **21**, 495.

<sup>10</sup> Hill, R. T., *Endocrin.*, 1937, **21**, 633.

<sup>11</sup> Deanesly, Ruth, *Proc. Roy. Soc. (Series B)*, 1938, **126**, 122.

<sup>12</sup> Lamar, J. K., *Anat. Rec.*, 1937, **70**, Suppl. p. 45.

<sup>13</sup> Greene, R. R., Burrill, M. W., and Ivy, A. C., *Endocrin.*, 1939, **24**, 351.

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<sup>1</sup> Witschi, E., Mahoney, J. J., and Riley, G. M., *Biol. Zentralb.*, 1938, **58**, 455.

<sup>2</sup> Price, Dorothy, *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 580.

always bilobed. One lobe, either the right or the left, may be present alone. Among the 46 cases of female prostates found in our colony, 17 had bilateral lobes and 29 had unilateral lobes. Of the latter, 25 had right lobes only and 4 had left lobes only. This greater frequency of right prostates in the female was also observed by Witschi and his coworkers and by Price. Among the bilateral female prostates found in our colony some showed inequality in the sizes of the two lobes. In all these cases the right lobe was larger than the left.

In a series of 17 ventral prostates from intact, immature females ranging in age from 20 to 36 days we found evidence of functional activity in 11, using presence of light areas in the acinar cells<sup>3</sup> as the criterion of function. Price<sup>2</sup> has shown that the female prostate develops in a manner which is essentially similar to that found in the young castrated male. Light areas (indicating secretory activity) appear in the female prostate at about 21 days and remain until about 40 days, after which the gland regresses as it does in the male castrate. Our observations, therefore, accord with those of Price on the functional state of the immature female prostate.

The fact that the prostates of the immature females show evidence of functional activity indicates that androgenic substances are being produced by the immature female. In order to locate the source of these androgens, it was decided to compare the state of the prostate in castrated and intact females. Because of the low incidence of female prostates in our colony the ventral prostates from littermate males were implanted into the females to serve as indicators of androgen production. The male prostates were implanted intraperitoneally into 36 intact and 36 castrated females at 10 days of age. The animals were killed at 20 to 35 days of age. Implants were recovered and ventral prostates, whenever present, were also removed. Both were fixed in Bouin's fluid, sectioned and studied microscopically. An interesting fact was brought out by this procedure. From the intact animals 16 implants were recovered. These were all non-functional. The 16 implants recovered from the castrate females were also negative. However, in 4 of the intact implanted females, the ventral prostates which were also present showed evidence of functional activity in spite of the negative condition of the implanted male prostates. The female prostate in the immature rat, therefore, appears to have a lower threshold of sensitivity to androgens than the male prostate as judged by the positive response of the female prostate and the negative response of the male prostate in the same

<sup>3</sup> Moore, C. R., Price, D., and Gallagher, T. F., *Am. J. Anat.*, 1930, **45**, 71.

animal. This finding differs from Price's observation in the adult rat<sup>2</sup> since she found (unpublished data) the female prostate to have a higher threshold of response. The age of the animal, however, may be a determining factor in the relative sensitivity of the male and female prostates.

Ventral prostates were also found in 10 castrated females, 6 from castrates with implants and 4 from an additional group of 20 castrates which had no implants. Four of these 10 ventral prostates showed some evidence of function, although the degree of activity was less than in the ventral prostates of the intact animals. This finding may not be considered significant because of the small number of cases, but nevertheless is indicative of some extra-ovarian source of androgens in the immature female.

In a previous publication the authors<sup>4</sup> have presented evidence that the prostate of the immature male castrate rat is maintained in a functional state by the adrenal. This andromimetic capacity of the male adrenal is evident only up to the age of 31 days, after which it diminishes, and is lost by 41 days.<sup>5</sup> Price<sup>2</sup> has suggested that the temporary functional state of the normal immature female prostate may also be due to the production of androgenic substances by the adrenal. The few cases which we have presented of functional activity in the prostates of castrate immature females tend to substantiate this hypothesis. Affirmation awaits further accumulation of data.

*Summary.* Ventral prostates from immature male rats were implanted into female litter mates, both intact and castrated, at 10 days of age. All implants were functionally negative when recovered 10 to 25 days later. Of the 27 female ventral prostates found in intact and castrated immature females, 15 showed some degree of functional activity. The data obtained indicate (a) that in the immature rat the female prostate has a lower threshold of response to androgens than the male prostate, and (b) that there is an extra-ovarian source of androgens in the immature female rat.

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<sup>4</sup> Burrill, M. W., and Greene, R. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 327.

<sup>5</sup> Burrill, M. W., and Greene, R. R., *Endocrin.*, 1940, in press.