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Androgenic Function of the Adrenals in the Immature Male Castrate Rat.*

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 adult male rat, castration invariably results in atrophy of the prostate within 4 or 5 days. In the immature male rat, however, castration is not accompanied by atrophy of the prostate. Price¹ found that the rat prostate will develop in an essentially normal manner in the absence of the gonads and that the functional integrity of the ventral prostate is maintained for a certain period after early removal of the gonads. Howard² confirmed Price's observations on the rat and suggested that a transitory andromimetic function of the adrenal may be responsible for the maintenance of the immature prostate in the absence of the testes. Davidson and Moon³ found that administration of adrenocorticotrophic substance to the immature castrated male rat caused hypertrophy of the adrenal cortex and also produced a gross and histological stimulation of the prostate.

The present experiment was undertaken to determine directly whether or not the immature male adrenal possesses an andromimetic function.

Immature male albino rats from our stock colony were used in the experiment. Litters were divided into 3 groups: (1) castrate at 16 days, (2) castrate at 16 days and adrenalectomized at 21 days, and (3) adrenalectomized at 21 days. All the animals were killed at 26 days of age. The ventral prostates were removed, fixed in Bouin's fluid, sectioned and stained with hematoxylin and eosin. An additional group of animals (not litter mates) were castrated at various ages (4 to 18 days) and killed at 26 days of age. Their ventral prostates were also removed and treated for microscopic examination.

All operations were done under ether anesthesia, particular care being taken to keep the anesthesia light for adrenalectomy. Powdered milk, bread, Purina dog checkers and 2% NaCl in tap water

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¹ Price, D., *Am. J. Anat.*, 1936, **60**, 79.

² Howard, E., *Am. J. Physiol.*, 1937, **119**, 339.

³ Davidson, C. S., and Moon, H. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 281.

were supplied to all the animals. Part of the litters were allowed to remain with the mother for the duration of the experiment inasmuch as the double shock of adrenalectomy and weaning appeared to increase mortality. The animals were generally in good condition when they were killed.

The normal ventral prostate of the mature rat consists of large acini with a delicate interacinous stroma. The acinar epithelium is composed of high, columnar cells with basal nuclei and characteristic light areas just distal to the nuclei. The presence of the light area which appears with ordinary fixation and staining technic and which represents the site of the Golgi body, has been accepted as the criterion for secretory activity of the prostate.⁴ The ventral prostate, following castration, presents a highly atrophic appearance: the acini are reduced in size, the stroma is apparently increased in amount, the epithelium is changed to a low, cuboidal type, sometimes scarcely wider than the nuclei, and the light areas are absent.

In the normal 26-day-old male, the ventral prostate presents an appearance which is practically identical with that of the normal adult except for the generally smaller size of the acini. After castration at various ages up to 21 days (Price), the prostates are temporarily maintained in a state which approaches the normal. The duration of this period of maintenance is dependent on the age at which castration is performed. According to Price, the prostate is maintained in a functional state for 10 to 20 days following castration between the ages of 16 to 21 days. The term "functional" applies mainly to the presence of light areas inasmuch as some atrophy of the gland may occur: the epithelium may be somewhat lower than normal, although not as low as in the adult castrate; the acini may be somewhat smaller than normal and the stroma may be slightly increased in amount.

In 18 adrenalectomized castrates, the ventral prostates consistently showed marked atrophy identical with that found in the adult castrate. In 6 adrenalectomized non-castrates the gland was histologically normal. In the 13 animals which were castrated but not adrenalectomized, the prostates were essentially normal in appearance. The height of the epithelium, size of acini and amount of stroma varied slightly in individual cases. The distribution of the light areas also varied somewhat. In the prostates of 4 of these castrate animals light areas were not found. However, none of the prostates of the plain castrates presented the true castration picture which was found in the prostates of the adrenalectomized castrates.

⁴ Moore, C. R., Price, D., and Gallagher, T. F., *Am. J. Anat.*, 1930, **45**, 71.

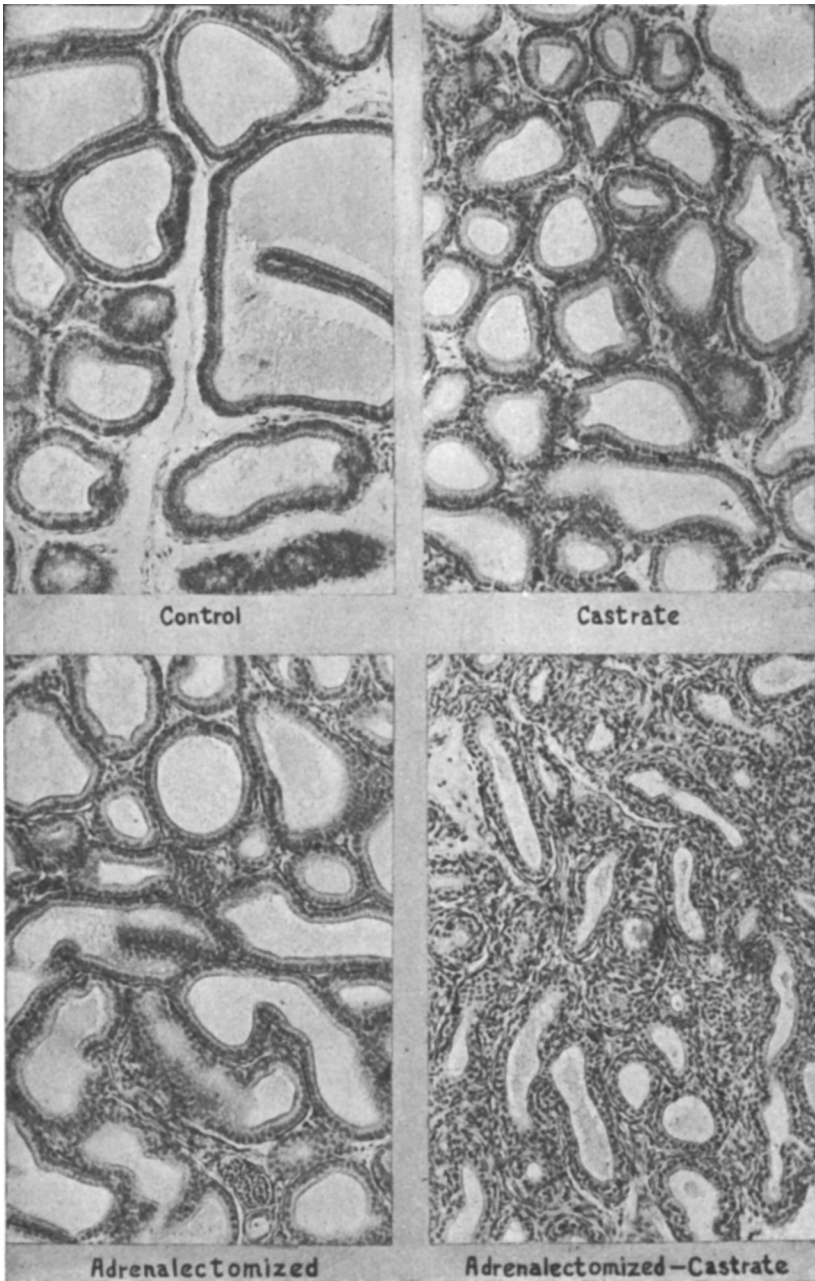


FIG. 1.
Sections of the ventral prostate.

In the 11 animals which were castrated at different ages (4 to 18 days), the prostates at 26 days of age were essentially normal in appearance. Some variation in the distribution of the light areas also occurred in these animals.

The experimental results clearly indicate that the adrenals of the immature male rat, in the absence of the gonads, are responsible for the maintenance of the ventral prostate gland in a normal or nearly normal condition. When the testes alone are removed, the prostate remains intact; when testes and adrenals are both removed, the prostate undergoes involution. That this latter effect is specific and not the result of general debility due to the adrenalectomy has been demonstrated inasmuch as removal of the adrenals alone produces no change in the prostates.

The fact that removal of the immature adrenals alone does not alter the condition of the prostate indicates that normally the adrenals are not appreciably involved in the development and maintenance of the prostate. The testes apparently produce sufficient androgen to maintain them. However, in the absence of the gonads, the immature adrenals are capable of maintaining the prostate in a "functional" state. This capacity of the adrenal apparently exists only in the immature animal since, after a certain age, prostatic atrophy always follows castration. How can this change be explained? Either the adrenal, in the course of its development, loses its andromimetic function or this function is retained, in which case the amount of androgen produced by the mature adrenal is probably insufficient to maintain the mature prostate. The latter alternative seems the more probable since certain substances having androgenic power have been isolated from the adult adrenals. Adrenosterone was isolated from the adrenal by Reichstein,⁵ who also showed that it has androgenic powers. Progesterone has been isolated from the adrenal by Beall and Reichstein.⁶ Its androgenicity has been established by Lamar⁷ and by Greene, Burrill and Ivy.⁸ The fact that other adrenal substances, such as corticosterone and desoxycorticosterone, are chemically similar to progesterone suggests that they also may be androgenic, at least to a slight degree.

⁵ Reichstein, T., *Helv. Chem. Acta*, 1936, **19**, 223.

⁶ Beall, O., and Reichstein, T., *Nature*, 1936, **142**, 479.

⁷ Lamar, J. K., *Anat. Rec.*, 1937, **70**, Suppl. p. 45.

⁸ Greene, R. R., Burrill, M. W., and Ivy, A. C., *Endocrinology*, 1939, **24**, 351.