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Effect of Testosterone Injections upon the Course of Pregnancy in Unoperated and in Castrated Rats.

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Since the male sex hormone testosterone* has become generally available, the current literature abounds in reports of its action in both the male and the female vertebrate. Among the various androgenic substances thus far isolated, testosterone most nearly resembles progesterone, hence in its action upon the reproductive tract it might also be expected to simulate that ovarian hormone.

Some experiments carried out at the Carnegie Laboratory corroborated the findings of others that testosterone causes a mucification of the vaginal mucosa and no cornification, and that in the monkey growth of the mammary tree and production of alveoli are stimulated by it. Markee (unpublished), working in the same laboratory in 1935-6, noted that testosterone, injected with estrin (Amniotin Squibb), antagonized the action of the latter in producing a reduction in the size of intraocular endometrial transplants, an effect which progesterone does not bring about. Hartman found that testosterone, like progesterone, prevented the appearance of an expected menstruation in the monkey, but, unlike progesterone, failed to cause any progravid changes in the endometrium.

From these experimentally determined facts it seemed theoretically possible that the injection of testosterone into a pregnant animal might well prevent parturition or abortion, even though the androgen might not replace progestin in other respects. Thus, in the rat, the abortion which always occurs after castration of the pregnant female, might well be prevented by testosterone and the injections so adjusted that delivery occurred at term. Or again, injection of the androgen towards the end of a normal pregnancy might be expected to postpone parturition, as happens with progesterone (King).

The results of 18 of the experiments carried out along these lines are recorded in Table I, from which the following conclusions may be deduced:

* It is a pleasure to record my thanks and that of the Department of Embryology, whose guest I have been during the past year, to the Ciba Company for a generous supply of Testosterone and Testosterone Proprionate manufactured by them.

TABLE I.

Animal No.	Date of Fertile Coitus	Date of Castration	Injections	Quantity inj. (mg.) daily*	Date of delivery	Days of Pregnancy	Condition of Fetuses
2	Jan. 29	—	Feb. 12-25	5	Feb. 26	28	Resorption and dead fetuses
1	Feb. 13	—	Mar. 5-9	5	Mar. 9	24	Living
5	Jan. 27	—	Feb. 10-21	5	Feb. 25	29	Resorption and dead fetuses
8	" 29	—	" 12-25	5	" 25	27	" " " "
4	" 28	Feb. 15	" 11-19	5	" 19	22	" " " "
7	Jan. 30	" 15	" 13-19	5	" 19	20	" " " "
11	" 28	" 15	" 13-19	5	" 19	22	" " " "
9	Feb. 23	Mar. 11	Mar. 10-20	5	Mar. 20†	25	Living
14	Mar. 9	—	" 27-30	5	Apr. 2	24	8 living, 4 dead fetuses
6	" 10	—	" 27-31	5	" 3	24	3 living, 3 dead fetuses
22	" 10	Mar. 27	" 27-30	5	" 1	22	Dead fetuses
16	" 9	—	" 27-30	2.5	" 3	25	3 dead
19	" 9	—	" 27-30	2.0	" 2	24	5 living, 3 dead fetuses
15	" 20	Apr. 2	Apr. 2-7	2.0	" 12	23	Resorption and dead fetuses
2§	Apr. 7	" 22	" 22-27	1.0	" 29	22	" " " "
8§	" 13	" 27	Apr.. 27-May 1	1.0	May 5	22	Dead fetuses
10	" 23	May 7	May 6-10	1.0	" 14	21	" "
16§	" 21	" 5	" 4-9	1.0	" 12	22	" "

*The first 8 rats of the table received the free Testosterone Ciba, the last 10 Testosterone Proprionate Ciba.
†Killed Mar. 20, 3 living fetuses found in utero.
§These 3 rats were used a second time, having conceived after the previous treatment with Testosterone.

1. Testosterone prevents or postpones parturition in the non-castrated pregnant female rat. If parturition does take place it is usually much delayed over the normal 21 days of gestation, which is the average for the strain used.

2. Testosterone is injurious to the embryos, probably through deleterious effect on the endometrium. Living embryos are to be expected only if injections are made for a short time towards the end of gestation. No. 9 of the table is exceptional.

3. Testosterone prevents the abortion which follows castration in the rat. A 5-day period of injection after castration will carry the fetuses to term, but only dead fetuses are usually delivered.

4. The larger the dosage, the more deleterious is the effect on the embryos. One milligram per day is sufficient to control the tendency of the uterus to empty itself.

5. The mode of action of testosterone on the pregnant uterus is not elucidated by the results presented in the table. The gross appearance of the uterus at autopsy argues for an excessive flaccidity of the uterine musculature.

6. The injection of testosterone in the amounts used in these experiments does not necessarily render the experimental animal sterile, for Nos. 16, 8 and 2 conceived 3, 7, and 6 weeks respectively after the treatment.

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Effects of Pinealectomy Over Several Generations.*

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Anderson and Wolfe[1] point out that previous results of pinealectomy have been almost equally divided among those authors who report premature sexual development, frequently accompanied by increased growth, and those who obtained negative results. In their own work on 30 rats, pinealectomized at 1-3 days with adequate controls, no effect was found on rate of growth, age of puberty or weights of endocrine organs involved in growth and sexual development.

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1 Anderson, D. H., and Wolfe, A., *J. Physiol.*, 1934, **81**, 49.