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Maintenance of Gestation in the Castrate Pregnant Rat with Androgens.*

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It is generally conceded that castration of the pregnant rat before the last few days of pregnancy results in termination of the pregnancy by resorption or abortion. Scipiades has demonstrated that pregnancy will continue after castration in this animal if testosterone or testosterone propionate are administered.[1] It is assumed that these androgens are able to maintain pregnancy because of their progesterone-like functions. Scipiades believes, however, that these androgens have a deleterious effect on the fetuses inasmuch as almost all of the offspring he obtained from treated mothers were born dead.

In the course of a study on the effects of androgens on embryonic sexual development, androgens have been administered to castrate pregnant rats in an attempt to eliminate the complicating factors of hormones produced by the maternal ovary. Some of these androgen-injected castrates have carried their pregnancies to term. Data concerning the effects of androgens on the course of pregnancy are presented here.

Thirty-one pregnant female rats were used in this study. The day of insemination was known for all animals. Castration was performed on the 8th to 14th day after insemination. The androgens were given daily in oil solution, starting on the day of castration, and continued to the 19th to 21st day of pregnancy. Parturition in the rats of our colony generally occurs on the 22nd day. Occasionally an animal delivers on the 21st day and rarely on the 23rd day. All animals were examined daily for vaginal bleeding and palpable progress of the pregnancy.

Twenty-five of these castrated pregnant rats were given testosterone propionate. In view of the fact that testosterone and androstenedione have been shown to have a weak progestational effect when tested in the rabbit,[2] these substances were used on the remaining 6 castrates. The number of animals used for this purpose was

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1 Scipiades, E., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 242.

2 Klein, M., and Parkes, A. S., *Proc. Roy. Soc. London*, 1937, **121**, 574.

TABLE I.

Substance	Day of castration	No. of animals	Daily dose, mg	No. resorbed	No. maintaining preg.	Avg No. of fetuses	
						Living	Dead
Test. Prop.	8-10	10	5-10	10	0	—	—
	11	3	5	2	1	4	0
	11	3	10-15	1	2	3	2
	14	9*	5	0	6	5.7	1.5
Testosterone	12	2	20	0	2	7	0.5
Androstenedione	14	2	10	1	1	3	1
	14	2	15	0	2	1	2

* Includes 3 mothers who died on the 19th or 20th days. Their fetuses are not included in the table.

limited by the relatively tremendous amounts of these substances necessary (180.0 mg testosterone, or 80.0-120.0 mg androstenedione to each animal).

Most of the animals were killed on the 22nd day. In the group of 14 day castrates treated with testosterone propionate 3 animals bled vaginally late on the 21st day and accordingly were killed. Three more died of unknown causes on the 19th or 20th day. These animals had 11, 12, and 13 healthy appearing fetuses *in utero* which were not included in the table.

The dosages used and the results obtained are presented in tabular form (Table I).

It is evident that certain androgens (testosterone, testosterone propionate and androstenedione) can substitute for the ovaries in maintaining pregnancy in the rat. Their effectiveness in this regard, however, seems to be limited by a definite time factor. All 10 of the animals castrated before the 11th day resorbed; only half of the animals castrated on the 11th day carried to term, while most of the animals castrated after the 11th day carried to term. Whether this time factor is absolute or is due to insufficient or excessive dosage cannot be determined on the basis of the known data.

Scipiades' conclusions that androgens are injurious to the fetus are not substantiated by our results. The average number of living young in our testosterone and 14 day testosterone propionate groups compare quite favorably with the average number of living young from normal animals of our colony (7.6 for 35 consecutive deliveries with a range of 2 to 13). Scipiades also concluded that "the larger the dosage, the more deleterious is the effect on the fetus." Our own data does not support this conclusion. He gave dosages of 1.0, 2.0, and 5.0 mg daily to 11 castrated pregnant rats and obtained living young only from one rat which had been given the

5.0 mg dose. Consequently we do not believe that his data support such a conclusion. It is our impression that, in the animals castrated after the 14th day, at least, the opposite is probably true, *viz.*, the fetal deaths are due to insufficient dosage.

We are therefore able to confirm the findings of Scipiades that androgens maintain gestation in the castrate rat, but are unable to confirm his conclusion that these androgens are injurious to the fetus.

Summary and Conclusions. Testosterone, testosterone propionate and androstenedione maintained pregnancy with resulting living fetuses in rats castrated during the latter half of pregnancy.

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Effects of Selective Salivary Gland Extirpation upon Experimental Dental Caries in the Rat.*

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The production of experimental tooth destruction seems to be one of the most valid methods by which oral pathology can be studied in the rat.[1] Although changes in caries-susceptibility have been obtained by the use of different diets it has not yet been adequately demonstrated whether the saliva plays a part in the observed effects. To test this relationship a procedure[2] for the extirpation of the salivary glands of rats has been reported which makes it possible to study the influence on the teeth of the removal of all or certain types of the salivary secretions. In this report various combinations of glands have been removed and the attending incidence of caries-susceptibility compared.

Experimental. A total of 88 rats were selected from the same Wistar breeding stock at 22 days of age and placed on two different diets. One of these (Hoppert, Webber, and Canniff[3]) was known

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1 Rosebury, T., *The Problem of Dental Caries, Dental Science and Dental Art* (S. Gordon, ed.), Philadelphia, Lea and Febiger, 1938.

2 Cheyne, V. D., *J. D. Res.*, 1939, **18**, 457.