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Maintenance of Pregnancy in Castrate Rats by Means of Progesterone.*

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Corner and Allen's[1] early successful attempts to maintain pregnancy in rabbits castrated shortly after mating could not be duplicated by Allen and Heckel[2] using crystalline progesterone, unless the castration occurred after implantation.[3] Pincus and Werthessen,[4] however, maintained gestation in one out of three rabbits when sufficient crystalline progesterone was used, while in short time experiments Courrier and Kehl[5] maintained pregnancy in rabbits with progesterone, but in only one rabbit was castration done before implantation. Courrier and Jost[6] using large amounts of pregneninolone caused rabbits to implant normally. Maintenance of pregnancy has been successfully accomplished in other animals (rats,[7, 8] ground squirrels,[8] mice[9] and hamsters[10]) using progestin,[8] progesterone[9, 10] or androgens,[7] when castration was done after implantation.

Previously[11] it was shown that placentomata indistinguishable from those formed in normal pseudopregnant rats could be produced in the castrate rat by means of progesterone alone. In the present study it will be shown that normal implantation as well as continued gestation will occur in the castrate rat when sufficient progesterone is administered.

A total of 26 pregnant rats were used, 22 of which were castrated on the 4th, and 4 on the 10th day of pregnancy. All rats, except

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1 Corner and Allen, PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 403.

2 Allen and Heckel, *Science*, 1937, **86**, 409.

3 Allen and Heckel, *Am. J. Physiol.*, 1939, **125**, 31.

4 Pincus and Werthessen, *Am. J. Physiol.*, 1938, **124**, 484.

5 Courrier and Kehl, *Comptes rendus Soc. de Biol.*, 1938, **128**, 188.

6 Courrier and Jost, *ibid.*, 1939, **130**, 1162.

7 Greene and Burrill, PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 585.

8 Johnson and Challans, *Endocrinol.*, 1932, **16**, 278.

9 Robson, *J. Physiol.*, 1938, **92**, 371.

10 Klein, Proc. Roy. Soc., B, 1938, **125**, 348.

11 Rothchild, Meyer and Spielman, *Am. J. Physiol.*, 1940, **128**, 213.

those in the first 2 experiments, were sterilized by ovario-salpingectomy of one horn of the uterus on the day after coitus, and the sterile horn traumatized by needle punctures through the antimesometrial wall on the 4th day of pregnancy. This permitted a concomitant study of the effect of the hormone treatment on the formation of placentomata. Hormone treatment was started on the day of complete castration, and continued daily up to and including the 20th day of pregnancy. All rats were autopsied on the 21st day, except in those cases where, by means of laparotomies performed between the 9th and 17th day, it was seen that pregnancy had terminated. Hormone treatment consisted of progesterone† alone, or in combination with estradiol,‡ with corn oil as the solvent.

From Table 1 it can be seen that negative results were obtained with amounts of progesterone of less than 1 Rb.U. per day. The smaller doses of progesterone, however, permitted the formation of implantation sites, which in the rats of Exp. I did not persist beyond the 13th day, but in 2 of the 4 rats of Exp. II persisted normally to

TABLE I.

Exp. No.	Daily hormone treatment		Rats treated	Rats maint. in pregn. to 21st day		
	Progest.*	Estradiol, γ		No.	Implant. Sites	Term Fetuses
I	.3	.03	4	0	—	—
II	.6	.03	4	0	—	—
III	1.0	—	5	2	5 5	1 1
IV	1.0	.15	3	1	2	1
V†	2.0	—	4	3	4 3 4	3 2 4
VI	2.0	—	5	4	2 3 4 4	1 2 3 1

* Rabbit units of progesterone.
†These rats were castrated on the 10th day of pregnancy.

† The source of progesterone was a non-crystalline preparation containing 10%-50% of progesterone (Corner-Allen Rabbit Units) and was made from cholesterol by the Spielman process. (Spielman and Meyer, *J. A. C. S.*, 1939, **61**, 893.)

‡ The estradiol was supplied through the courtesy of the Schering Corporation, Bloomfield, N. J.

the 17th day. Implantation proceeded normally, as far as could be determined macroscopically, in all the remaining experiments, and at least some of the rats in each experiment carried living young to the 21st day. The percentage of completely maintained rats, as well as the ratio of living young to total number of implantations, increased with increase in the amount of progesterone administered.

The placentomata which formed in the sterile horn of the uteri of all the rats of Exp. III-VI were larger in every case than the implantation sites in the pregnant horn. This would indicate that the formation of decidual tissue in the rat is dependent, not only upon the size of the progesterone dose,[11] but possibly upon the strength of the traumatic stimulus as well, since it is most likely that the trauma of the uterine epithelium produced by the implanting egg is not of the same order of magnitude as that used in the artificial production of placentomata.

The possibility that contaminants in the progesterone preparation might have influenced the results must be admitted, but we do not believe that they played an important part. In other experiments,[11, 12] using the same type of preparations, we found no quantitative or qualitative differences between the non-crystalline and crystalline progesterones.

Summary. Rats castrated on the 4th day of pregnancy were maintained in pregnancy until the 21st day with daily doses of progesterone of 1 or 2 Rb.U.

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Precipitation Pattern of Serum Proteins in Phenylpyruvic Oligophrenia.

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Jervis, *et al.*,[1] have shown that the serum of phenylpyruvic oligophrenic individuals contains an abnormal amount of phenylalanine. In view of the recognized effects of small amounts of amino acids on the molecular dispersion of the proteins[2] it seemed possible that

12 Rothchild and Meyer, *Anat. Rec.*, 1939, **75**, supl. 1, 71.

1 Jervis, G. A., Block, R. J., Bolling, D., and Kanze, E., in press.

2 Tiselius, A., *Ann. Rev. Biochem.*, 1939, **8**, 155.