13059 P

Maintenance of Pregnancy in the Hypophysectomized Rat.‡

EUGENE CUTULY.

From the Department of Anatomy, Wayne University College of Medicine, Detroit.

Evidence is accumulating that a factor closely associated with the lactogenic principle of the anterior pituitary may be responsible for functional maintenance of the corpus luteum.[1-4] The following data lend support to this concept.

Numerous unsuccessful attempts to maintain pregnancy in the hypophysectomized rat with pregnant mare serum (PMS)* led to a trial of other preparations, including lactogenic hormone (LCH),*† a hypophyseal gonadotropic synergist (SY),* and whole anterior pituitary extract (WAP).† Results and relative data appear in Table I. Hypophysectomy was performed between days 5 and 12 of gestation. Pregnancies maintained in rats hypophysectomized prior to the 11th day of gestation may be considered as evidence of successful hormone treatment, since ablation of the hypophysis before the 11th day will terminate pregnancy,[5] owing to atrophy of the corpus luteum.

Of 15 hypophysectomized animals pregnancy was not maintained in 7. Four of the failures were treated with PMS (1 or 2 R.U. daily) and 3 were treated with LCH (2 or 3 mg daily). It should be noted that one of the latter 3 (No. 5) was hypophysectomized only 5 days after mating, and before the expected time of implantation of the fertilized ova.

Pregnancy was maintained in 8 animals from which the pituitary had been removed 7-9 days after mating. LCH (2-3 mg daily) caused maintenance in 6 instances, and SY (3 mg daily) and WAP

‡ This study was aided in part by Works Project Administration No. 665-51-3-225.

1 Dresel, I., *Science*, 1935, **82**, 173.

2 Lahr, E. L., and Riddle, O., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 880.

3 Evans, H. M., Simpson, M. E., and Turpeinen, K., *Anat. Rec.*, 1938, **70** (suppl.), 26.

4 Pfeiffer, C. A., *Anat. Rec.*, 1941, **79** (suppl.), 50.

* Pregnant mare serum, hypophyseal synergist, and some lactogenic hormone were supplied by Dr. Erwin Schwenk, Schering Corp., Bloomfield, N.J.

† Most of the lactogenic hormone and the whole anterior pituitary extract used in this work were supplied by Dr. J. B. Schooley, Difco Laboratories, Inc., Detroit, Mich. Thanks are also due Dr. Schooley for his help in obtaining 4 pregnant rats.

5 Pencharz, R. I., and Long, J. A., *Am. J. Anat.*, 1933, **53**, 117.

TABLE I.
Effect of Chorionic Gonadotropin and Anterior Pituitary Extracts on Maintenance of Pregnancy in Hypophysectomized Rats.

Rat No.	Days pregnant at time of hypophysectomy	Treatment: Substance	Daily dose in 1 cc of vehicle	No. of days continued	Litter born (days after mating)	No. of young in litter	Adrenals (g)
1	12	PMS	2 R.U.	14	—	—	—
2	9	"	1 "	13	—	—	—
3	8	"	2 "	15	—	—	—
4	8	"	2 "	8	—	—	.030
5	5	Prolactin No. 35*	3 mg	17	—	—	.022
6	8	" S‡	3 "	15	—	—	.021
7	8	" 35	2 "	16	—	—	.035
8	7	" No. 35771 C†	3 "	17	22	5	.024
9	7	Prolactin S	3 "	17	24	§	.022
10	8	" No. 35	2 "	14	23	8	.029
11	9	" "	2 "	13	22	7	.036
12	9	" "	2 "	13	22	7	.035
13	9	" No. 35771 C	2 "	14	23	7	.044
14	7	Synergist	3 "	17	‖	10 (dead)	.030
15	9	Whole AP	2 "	16	‖	6	.035
16	Normal	—	—	—	22	9	.071
17	"	—	—	—	22	4	.062

*Prolactin (No. 35) was a Difco lactogen assaying 10 I.U. per mg and free of luteinizing hormone.
‡Prolactin (S) was a Schering lactogen.
†Prolactin (No. 35771 C) was a Difco lactogen assaying 20 I.U. per mg and ¼ unit of luteinizing hormone.
§Litter eaten at birth.
‖Not delivered after 26 days.

(2 mg daily) were successful in the one case where each was used. Presumably the corpus luteum—stimulating factor, which Astwood[6] has termed luteotrophin, was present not only in whole anterior pituitary extract, but also in purified lactogenic and gonadotropic synergist fractions.

It will be observed that normal delivery of litters occurred on days 22, 23, or 24 of gestation despite continuation of hormonal administration, except in 2 instances. The rats treated with WAP and SY did not deliver. The former died 26 days after mating and the latter, in a weakened condition, was killed 27 days after mating. Whether any significance can be attached to the fact that these animals did not deliver, while lactogen-treated animals did, will have to be determined by further studies.

When pregnancy was maintained mammary glands revealed slight

[6] Astwood, E. B., *Endocrinology*, 1941, **28**, 309.

to marked degrees of stimulation. Lactation was scanty or entirely lacking, and litters died 1 or 2 days after birth. The adrenals of some of the animals treated with LCH were somewhat stimulated as indicated by their weights, while others were atrophic.

Summary. Pregnancy in rats hypophysectomized on or before the 9th day of gestation was maintained with lactogenic hormone, pituitary gonadotropic synergist, and whole anterior pituitary extract. Each of these substances maintained pregnancy presumably by its ability to stimulate function of the corpus luteum.

13060 P

A Natural Antibody Reacting with Sedimentable Constituents of Normal Tissues.

JOHN G. KIDD AND WILLIAM F. FRIEDEWALD.

From the Laboratories of The Rockefeller Institute for Medical Research, New York City.

While making serological studies of several transplanted rabbit cancers by the methods that disclosed a distinctive substance in the Brown-Pearce carcinoma,[1] we have noted that the blood serum of normal rabbits will fix complement in mixture with saline extracts of normal rabbit tissues in dilutions far beyond any anticomplementary or summative effects. This phenomenon appears to be due to a natural antibody that reacts with sedimentable constituents of normal tissues.

The antibody can be detected by means of a standardized complement fixation test in which 2 units of complement are employed and 2 hours at room temperature allowed for fixation. Antigens are prepared by extracting normal rabbit tissues (liver, kidney, brain, etc.—either fresh or preserved frozen at −22°C) with sand in a mortar, suspending the ground paste in physiological saline (1:10 to 1:40 or more) and centrifuging at 4400 rpm for 20 minutes. The unheated supernatant liquids, opalescent but free from gross particles, have proved notably effective in the tests.

When the sera of 22 normal adult rabbits were mixed with antigens consisting of 1:20 or 1:40 saline extracts of normal rabbit livers, fixation invariably occurred, and it was complete with many of the sera in dilutions as high as 1:16 to 1:64. No fixation was

[1] Kidd, John G., *J. Exp. Med.*, 1940, **71**, 335, 351.