

per 226.9 g of tissue; the female one I. U. per 371.5 g. Only two birds were used for each test and the difference in response was in one case about 100%, in the other about 50%. Lack of material prohibited the use of more birds.

While the experiments give positive evidence of androgens in the placenta, they may not be taken as quantitative. The wide variation between the colorimetric test and the capon assay is confusing, but may be related to the relative amounts of androgens or 17 ketosteroids. No effort was made to determine which of the 17 ketosteroids were present.

It is rather interesting, although it may not be significant, that the male placenta contains considerably more hormone, by both tests, than the female.

### 13306

#### **Implantation Following Mating in Hypophysectomized Rats Injected with Lactogenic Hormone.\*†**

EUGENE CUTULY.

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

In a recent article<sup>1</sup> the writer reported that lactogenic hormone, hypophyseal synergist, and whole anterior pituitary extract maintained pregnancy in rats hypophysectomized after implantation of fertilized ova had occurred. The data which follow may show that nidation and subsequent development of fertilized ova will occur in hypophysectomized rats under the influence of lactogenic hormone.

Fourteen experimental animals were used. Time of mating was determined by the presence of a copulation plug in the vagina or of sperm observed in the vaginal smears. Vaginal examinations were made at 4:00 p.m. and 10:00 a.m., so the exact time of coitus, which always occurred in the intervening 18-hour period, was not

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† Most of the lactogenic hormone used in this work was supplied by Dr. Erwin Schwenk, Schering Corporation, Bloomfield, New Jersey. Some of the lactogenic hormone was supplied by Dr. J. P. Schooley, Difeo Laboratories, Inc., Detroit, Michigan.

<sup>1</sup> Cutuly, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **47**, 126.

known. If vaginal examination showed that coitus had occurred during this interval, the female was considered to be 1 day pregnant, even though fertilization could not have occurred more than 18 hours previously. In many instances, in fact, it is probable that signs of coitus were discovered very shortly after mating, as frequently large numbers of motile sperm were found in the vaginal smears. Since hypophysectomies were never performed after 4:00 p.m., it follows that the interval between mating and hypophysectomy (Table I, column 2) was invariably shorter than indicated. The method described for determining inception of pregnancy has been employed by the writer for a number of years on a large number of normal rats. Its accuracy is indicated by the fact that delivery in such animals has almost without exception occurred on the 22nd day post coitum; *i. e.*, 21 days after discovery of sperm in the vagina.

In 4 animals (Nos. 1-4) injected with lactogenic hormone<sup>2</sup> (1-3 mg daily) implantation did not occur.

In 8 animals (Nos. 6-13) in which implantation was successful,

TABLE I.  
Influence of Lactogenic Hormone on Rats Hypophysectomized at Pre-implantation Stages of Pregnancy.

| Rat No.                               | Hypophysectomy (days) | Treatment |                    |                       | First blood in vagina, days after mating | Pregnancy maintained days after mating | No. in litter | Autopsy data |               |
|---------------------------------------|-----------------------|-----------|--------------------|-----------------------|------------------------------------------|----------------------------------------|---------------|--------------|---------------|
|                                       |                       | Substance | Daily dose in 1 cc | No. of days continued |                                          |                                        |               | Ovaries (mg) | Adrenals (mg) |
| 1                                     | 4                     | SL*       | 1                  | 19                    | 0                                        | 0                                      | 0             | 27           | 27            |
| 2                                     | 3                     | SL        | 3                  | 16                    | 0                                        | 0                                      | 0             | 44           | 41            |
| 3                                     | 1                     | SL        | 3                  | 16                    | 0                                        | 0                                      | 0             | 25           | 29            |
| 4                                     | 2                     | SL        | 3                  | 19                    | 0                                        | 0                                      | 0             | 30           | 30            |
| 6                                     | 5                     | DL35†     | 3                  | 18                    | 10                                       | 9                                      | 0             | 33           | 22            |
| 7                                     | 4                     | SL        | 3                  | 18                    | 10                                       | 9                                      | 0             | 21           | 31            |
| 8                                     | 3                     | DL35      | 1                  | 17                    | 7                                        | 6                                      | 0             | 32           | 27            |
| 9                                     | 4                     | SL        | 3                  | 15                    | 10                                       | 9                                      | 0             | 26           | 31            |
| 10                                    | 3                     | SL        | 1                  | 11                    | 10                                       | 9                                      | 0             | 29           | 33            |
| 11                                    | 3                     | SL        | 3                  | 10                    | 11                                       | 10                                     | 0             | 31           | 38            |
| 12                                    | 4                     | SL        | 3                  | 14                    | 12                                       | 17                                     | 8             | 31           | 30            |
| 13                                    | 1                     | SL        | 3                  | 19                    | —                                        | †                                      | 10            | 50           | 40            |
| 15                                    | 3                     | DL786B§   | 3                  | 20                    | 13                                       | 23                                     | 7             | 42           | 33            |
| 16                                    | 3                     | SL        | 3                  | 23                    | 12                                       | 25¶                                    | 8             | 49           | 36            |
| Avg of 4 normal pregnant controls     |                       |           |                    |                       | 13                                       | 22                                     | 7             | 75           | 65            |
| Avg of 7 normal non-pregnant controls |                       |           |                    |                       |                                          |                                        |               | 69           | 61            |

\*SL = Schering Prolactin, assaying 12½ I.U. per mg.

†DL35 = Difco Prolactin, assaying 10 I.U. per mg.

‡At autopsy small well formed fetuses were found. Possibly implantation was delayed.

§DL786B = Difco Prolactin, assaying 10 I.U. per mg.

||Young dead at birth.

¶Rat died without delivering.

pregnancy was interrupted 6 to 17 days after impregnation. Hypophysectomy was performed 1 to 5 days after mating, and the animals were treated with lactogenic hormone (1-3 mg daily). In all but one (No. 13) resorption of embryos or fetuses was in progress at the time of autopsy. Unfailing evidence that resorption was under way was provided by the presence of blood in the vagina prior to the expected time of the "placental sign," and by pronounced and progressive loss in body weight. In the table the beginning of fetal resorption is given as one day prior to the appearance of blood. This arbitrary figure might not be correct in all instances, but it serves as a relative measure of time during which pregnancy was maintained in the group of animals. At autopsy, swellings of various sizes were seen along the uteri. These sites were found to contain hematomata surrounding embryos or fetuses and sometimes placentae which had undergone different degrees of degeneration. Rat No. 13 deserves special mention. It had lost weight after operation, although it showed sporadic small gains. Except for a faint brownish coloration in the vaginal mucus 17 days after mating, no blood was observed when vaginal smears were made. On post coital day 21 the animal was killed. Five swellings were found in each uterine horn, which upon dissection revealed well formed fetuses of different sizes. These were judged to be comparable to normal fetuses of 9 to 12 days of age. Possibly implantation had been delayed.

In 2 animals (Nos. 15 and 16), hypophysectomized 3 days after mating, pregnancy was continued to term (No. 15) or beyond term (No. 16) under the influence of lactogenic hormone (3 mg daily). Rat No. 15 delivered 7 dead fetuses on day 23 of pregnancy, while rat No. 16 died 25 days after mating without delivering. At autopsy 8 large dead fetuses were found in the uterine horns. The mammary glands in both cases were highly developed and the ovaries contained large healthy corpora lutea.

Ovarian weights were low compared with normal values. This would seem to indicate lack of stimulation except possibly that of previously formed corpora lutea. On the basis of weight, it seems possible that the adrenal glands of some of the treated animals were slightly stimulated. This matter, however, must be investigated more thoroughly before the heavier weights of some of the glands can be considered significant.

The results presented, together with those recently published,<sup>1</sup> leave no doubt that lactogenic hormone is capable of stimulating function of the corpus luteum. Evans and coworkers<sup>2, 3</sup> have

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<sup>3</sup> Evans, H. M., Simpson, M. E., Lyons, W. R., and Turpeinen, K., *Endocrinology*, 1941, **28**, 933.

illustrated this action of lactogenic hormone by production of deciduomata in hypophysectomized rats, and Astwood<sup>4</sup> has employed mucification of the vagina in immature rats as a means of demonstrating the same effect. When gonadotropic substances<sup>1</sup> are employed in attempts to stimulate function of the corpus luteum, the question of dosage must be regarded as highly important. Dosage of a gonadotropin which can cause follicular as well as luteal development is difficult to regulate. If the dose is low only follicles form; if the dose is high both follicles and corpora lutea develop. Demonstration of luteal function in such instances is difficult since the output of estrogen would tend to override effects of luteal hormone. Until such problems are more thoroughly investigated, therefore, it does not seem wise to reject the view that some gonadotropins which cause formation of corpora lutea may also cause the corpora to function.

*Summary.* Fourteen rats, hypophysectomized 1 to 5 days after mating, were injected with lactogenic hormone (1 or 3 mg daily). In 4 animals implantation failed to occur. Of the remaining 10 animals 2 carried to term or beyond, while pregnancy was interrupted after 6-17 days in 8 rats. It would seem that lactogenic hormone was capable of stimulating corpus luteum function sufficiently to induce implantation and to maintain pregnancy for periods ranging from 6 days to term or beyond.

## 13307

### Chemotherapy of Lymphogranuloma Venereum with Sulfonamide Drugs.

HELEN P. JONES, GEOFFREY RAKE AND CLARA M. MCKEE.

*From the Squibb Institute for Medical Research, New Brunswick, N.J.*

It was recognized early that in lymphogranuloma venereum, unlike most other virus diseases, some success attended treatment of infected mice or guinea pigs with drugs of the sulfonamide group. The earlier work has been summarized by Findlay.<sup>1</sup> In a previous communication from this laboratory<sup>2</sup> it was indicated that,

<sup>4</sup> Astwood, E. B., *Endocrinology*, 1941, **28**, 309.

<sup>1</sup> Findlay, G. M., *Lancet*, 1940, **2**, 682.

<sup>2</sup> McKee, C. M., Rake, G., Greep, R. O., and van Dyke, H. B., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 417.