

of the interstitial tissue. This hypertrophy was characterized by masses of compact, lightly staining cells which resembled, at least superficially, the "luteal cells" of the bird ovary. A more detailed cytological study is now in progress.

These experiments show that chick testes were only moderately stimulated by F.S.H. when such hormone was made available by implantation of pituitaries from castrate rats, and that female pituitaries elicited the greatest physiological response. Several factors may be suggested as influencing these results: (1) possible deleterious effect of the temperature which is about 5°F. higher in the bird; (2) greater weight of the female pituitary gland of the rat; and (3) failure to get an adequate "take" of the gland due either to place of implantation or to the fact that foreign protein was introduced. These variables are being investigated as far as possible.

### 8986 C

#### **Tolerance of the Rhesus Monkey to Pituitrin Injections and Absence of Uterine Bleeding Following Injection.**

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The following experiments were performed to test the possible rôle of pituitrin in the causation of menstrual bleeding. Incidentally the high tolerance of the Rhesus monkey to pituitrin was demonstrated.

By observing the vascular phenomena in intra-ocular transplants of the endometrium Markee<sup>1</sup> has shown that the most constant feature of menstruation is the constriction of the spiral arterioles of the functionalis layer. In view of the further finding of Hartman and Firor<sup>2</sup> that menstrual bleeding could be elicited in monkeys from which the anterior but not the posterior pituitary had been removed, it seemed reasonable to suppose that pituitrin might be responsible for the vasoconstriction that leads to necrosis and sloughing of the functionalis in menstruation.

Preliminarily, a number of female monkeys were injected with large doses of pituitrin to determine tolerance as well as the effect

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<sup>1</sup> Markee, J. E., *Anat. Rec.*, 1936, **64**, 32.

<sup>2</sup> Hartman, C. G., and Firor, W. M., *Anat. Rec.*, 1935, **61**, 55.

of the drug on the sex color, which has also been shown to be a vascular phenomenon. Two experiments are cited.

*Monkey No. 7*, 15-year-old female having constantly red buttocks and nipples, shade No. 9 on a color scale of 10. Bleedings occurred on September 19, November 1, 1934, and January 31, 1935. On December 11, 1934, five units of pituitrin were injected intravenously. Clotting of blood was prevented by the use of a calculated amount of heparin. In 3 minutes the color of nipples and sex skin had dropped to 7; in 4 minutes to 6; in 7 minutes to 4. In 12 minutes it was back to 7.

*Monkey No. 108*, old female, buttocks constantly red—9 on a scale of 10. On December 11, 1934, day 7 of the cycle, 10 units of pituitrin were injected intravenously. The right and the left sides of the sex skin blanched at different rates, as follows: in 2 minutes, 7 and 6 respectively; in 3 minutes, 6 and 4; in 5 minutes, 5 and 3; in 6 minutes, 4 and 2. Although the injection was made into the right saphenus vein it was the left half of the sex skin that suffered the greater blanching.

No uterine bleeding followed such momentary action of the drug, nor was any expected, since Markee had determined that the period of continuous blanching lasts 6 to 20 hours before the menstrual bleeding begins. Accordingly 3 females were injected by a continuous "drop" method over a period of 5 hours in each case. A cannula was placed in the saphenus vein and connected with a burette by means of a thin-walled rubber tube. The pituitrin was dissolved in 100 cc. physiological saline and delivered to the blood stream at the rate of 3 cc. in one minute. The animals were anesthetized with Nembutal (Abbott), initial dose 0.4 grain per kilo body weight, supplemented when necessary with further injections of 0.25 grain by means of a hypodermic needle run through the rubber delivery tube. The animal was covered with toweling and the operating table was slightly warmed from below with an incandescent light bulb.

Non-ovulating females were selected in order to avoid the possible inhibiting action of progesterone on the reactivity of the arterioles.

I. *Rhesus Female No. 256*; weight 5200 gm.; injected on February 20, 1935, day 19 of the menstrual cycle, from 10:20 A. M. to 3:25 P. M. During this period the enormous amount of 464 units of pituitrin (232 mg.) was delivered. A total of 4.25 grains of nembutal was necessary to "hold" the animal, an amount considerably above the minimal lethal dose (about 0.6 grain per kilo)

if injected at one time. At 11:00 A. M. and at 2:14 P. M. the rectal temperature was 102.6°F., the pulse rate 170.

II. *Rhesus Female No. 217*; weight 4400 gm., very "regular" in menstruation though never ovulating. Bleedings January 16, February 11, March 7, April 3, 1935. Injected on March 5 (10:35 A. M. to 3:34 P. M.), with a total of only 4.4 units of pituitrin and 2.51 grains of nembital. At 11:30 the rectal temperature was 100°F., the pulse rate 140.

III. *Bonnet Female (Macaca radiata) No. 147*; adult, castrated in February, 1932, body weight 3660 gm. She had received 100 R.U. estrin (Amniotin. Squibb) daily for more than 3 months until March 8, 1935. Injection of pituitrin was made on March 12 on the theory that 4 days after cessation of estrin injections uterine bleeding might be precipitated with the 15 units of pituitrin used. Bleeding did not occur until March 25.

In none of these injected animals was uterine bleeding hastened by the injections of 4.4, 15 or 454 units of pituitrin.

The usual anuria accompanied the injections.

## 8987 C

### Virulence in Relation to Early Phases of the Culture Cycle.

FRIEDA OFFENBACH. (Introduced by C.-E. A. Winslow.)

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In view of the many physiological characteristics of bacteria which have been found to vary in different phases of the culture cycle, it was thought worth while to see if virulence for the animal host would also show correlation with "physiological youth."

A strain of *Salmonella enteritidis* (pathogenic for mice by mouth) was cultivated in a one per cent peptone medium continuously aerated with the apparatus devised in this laboratory by H. H. Walker. The lag-period of this organism in this medium was one hour and the period of logarithmic increase extended from the second to the sixth hour with decline setting in after the eighth hour.

Cultures in the first, fifth and sixth hours were used for the intra-abdominal injection of 95 mice, one cc. amounts containing either 10,000 or 100,000 organisms being employed. All mice died in periods varying from one to 15 days. The mean time of survival was as follows: