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Production of Placentomata in Rats Injected with Anterior Hypophyseal Fluid.

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Evans and Long[1] have reported that in rats injected with extract of anterior lobe of the hypophysis of beef, oestrus may never occur, or occur only at long intervals. The ovaries of such animals weighed twice as much as in control animals, showing the presence of very abundant lutein tissue and the absence of normal Graafian follicles. Teel[2] was able to prove that this lutein tissue is functional as regards its ability to sensitize the uterine mucous membrane, as determined by the placentoma reaction of L. Loeb.[3] The uterine mucous membrane of injected animals exhibits the decidual cell reaction 5 or 6 days after the beginning of the treatment.

However, this typical reaction can be obtained only during a short period of the life of the corpora lutea, as shown by the following experiments:

Group I. Female rats, which were having normal cycles, were injected daily with anterior hypophyseal fluid. On the day of the fifth injection, a loop of silk thread was inserted through the lumen of the uterus to produce an injury to the uterine mucosa. Between the fourth and the seventh days after operation, the animals were killed. No cycle occurred during the experiments. In every animal large placentomata were found in the injured uterine horn, not exclusively limited to the sites of injury, but including in some cases almost the total length of the horn. The ovaries contained in each case numerous corpora lutea and were larger than in a normal animal. Some of these ovaries exhibited the typical aspect described by Evans and Long as "mulberry ovaries." This first group of experiments confirm the results of Evans and Long and of Teel.

Group II. Loops of silk thread were inserted through the lumen of the uterus of female rats at different periods of the oestrous cycle. Daily injections of anterior hypophyseal fluid were made, starting on the day following operation, and the animals were sacrificed after 5 to 12 injections. In some animals a very slight tumefaction was found at the sites of injury; other animals did not exhibit any reaction. In no cases were typical large placentomata obtained. However, the oestrous cycle was stopped during injections and the

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ovaries contained large and numerous corpora lutea. These experiments seem to indicate that large placentomata can be obtained only after the uterine mucosa has been sensitized by the action of the corpora lutea.

Group III. Female rats were injected daily with hypophyseal fluid. On the day of the 10th injection, loops of thread were inserted, and the animals received 5 daily injections after the operation. In no case was the placentomata reaction observed. The same negative results were obtained in animals injected daily, injured by loops of thread on the 23rd to the 27th day of treatment and injected for 5 to 18 days after operation. In this group also, the oestrous cycle was inhibited during the experiments; the ovaries contained numerous corpora lutea and some were typically "mulberry ovaries."

These experiments can be explained by the experiments of Hisaw,[4, 5] and Weichert.[6] The first author showed that corpus luteum extract produces a relaxation of the pubic symphysis of the castrated guinea pig, only when the animal is under the influence of the follicular hormone. Injecting the same extract, Weichert was able to produce placentomata in spayed rats, but only after the animal was put in artificial oestrus by follicular hormone.

It seems that the reason it is not possible to obtain the placentomata in animals injected with hypophyseal extract and presenting persistent corpora lutea for 10 days or more is because they are too far away from the last oestrum and consequently not under the influence of the follicular hormone. In such conditions the uterine mucosa can not react to a stimulus by producing decidual cells.

Conclusions. 1. In animals injected daily with anterior hypophyseal fluid, and presenting numerous persistent corpora lutea, it is possible to obtain regularly large placentomata if the injury of the uterine mucosa is produced around the fifth day of injections and the animal killed 5 to 7 days after operation.

2. If the injury of the uterine mucosa is made the day before the injections started, it is not possible to obtain large placentomata. A slight enlargement at the sites of injury may be observed.

3. If the injury of the uterine mucosa is made after 10 days or more, placentomata are never obtained.

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[2] Teel, H. M., *Am. J. Physiol.*, 1926, lxxix, 184.

[3] Loeb, L., *Zentralbl. f. Physiol.*, 1919, xxiii, 73.

[4] Hisaw, F. L., unpublished. Reported A. A. A. S., Nashville, 1927.

[5] Hisaw, F. L., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 661.

[6] Weichert, C. K., PROC. SOC. EXP. BIOL. AND MED., 1928, xxv, 490.