## ACTION OF PROGESTERONE ON MITOTIC INDEX IN THE EPITHELIUM OF THE UTERINE WALL, UTERINE GLANDS, AND VAGINA

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A single injection of 0.05, 1.0, and 2.5 mg progresterone into ovariectomized mice causes a marked increase in the mitotic index in the epithelium of the uterine wall, uterine glands, and vagina. A single injection of 2 mg progesterone increases the mitotic index in the epithelium of the uterine glands 24 h after injection, and in the epithelium of the uterine wall and vagina 30 h after injection.

\* \*

Previous experiments on rabbits and mice showed that repeated injection of progesterone, without preliminary administration of estrogens, increases mitotic activity in the epithelium of the uterus, vagina, and mammary glands [1-5].

The object of the present investigation was to determine whether a single injection of progesterone changes the mitotic index (MI) of the uterine and vaginal epithelium in ovariectomized mice.

## EXPERIMENTAL METHOD

Experiments were carried out on noninbred mice with a mean weight of 26 g, ovariectomized 26 days before the beginning of the experiment. The animals were divided into four groups (5 in each group): the mice of group 1 received 0.1 mg progesterone\*, group 2 0.5 mg, group 3 1.0 mg, and group 4 2.5 mg. The mice were sacrificed 27 h after injection. In a preliminary experiment carried out to choose the optimum times of sacrifice of the mice after a single injection of hormone, 26 mice were injected with 2 mg progesterone each, and these animals were sacrificed after 6 (5 mice), 24 (5 mice), 30 (5 mice), 48 (5 mice), and 56 (6 mice) h. Mitoses were counted in the epithelium of the uterine wall and vagina in 3000 cells,

and in the epithelium of the uterine glands in 1000 cells. Mitoses in the vagina were counted only in the stratum basale.

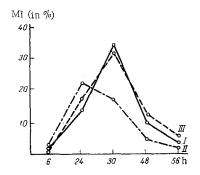


Fig. 1. Changes in MI in epithelium of uterine wall (I), uterine glands (II), and vagina (III) of ovariectomized mice 6, 24, 30, 48, and 56 h after a single in-jection of 2 mg progesterone.

## EXPERIMENTAL RESULTS

In a preliminary experiment the maximum number of mitoses in the epithelium of the uterine glands was observed after 24 h, and in the epithelium of the uterine wall and vagina after 30 h (Fig. 1).

As the writer has shown by earlier experiments, and also according to data in the literature, only solitary mitoses are observed in the epithelium of the reproductive organs of ovariectomized mice. The vaginal and uterine epithelium of ovariectomized mice is considerably flattened and becomes cubical. The nuclei are frequently pycnotic. The uterine

\*An oily solution of progesterone (Rostov Factory, Batch No. 30,3687) was used in the experiments.

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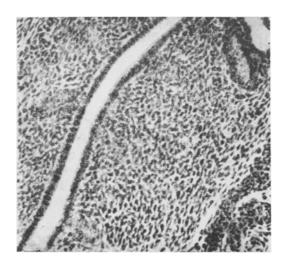


Fig. 2. Uterine epithelium of ovariectomized mouse.

TABLE 1. Action of Progesterone on MI of Epithelium of Uterine Wall, Uterine Glands, and Vagina of Ovariectomized Mice

	<u>-</u> i	Mean number of mitoses (in $^{0}/_{00}$ )		
Dose of progester one (in n	No. of an mals in group	uterine walls	epithelium of uterine glands	epithelium of vagina
Con- trol	25	1,0	1,5	0,5
0,1 0,5 1 2,5	5	0,9 (0,33—1,0) 32,3 (18,0—43,6) 28,5 (13,6—48,3) 33,1 (12,0—51,3)	24,6 (10,0-48,0)	37,5 (32,5-42,6)

Note. Limits of variations of MI in group given in parentheses.

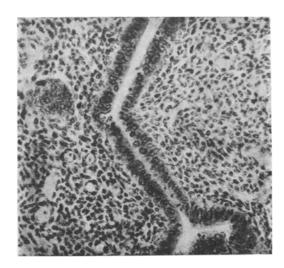


Fig. 3. Uterine epithelium after a single injection of 1 mg progesterone.

epithelium has a smoothed relief, and the uterine glands are considerably reduced (Fig. 2). A single injection of 0.5, 1.0, and 2.5 mg progesterone led to a significant increase in MI in the epithelium of the uterus, uterine glands, and vagina (P=0.01, 0.001, 0.001; Table 1). No significant difference was found between the results of the action of these three doses of hormone. All that can be said is that the fluctuations in MI after administration of large doses were somewhat more marked. The histological structure of the uterine and vaginal epithelium was considerably modified. The vaginal epithelium became stratified, the uterine epithelium became high, cylindrical in type, with a complex relief (Fig. 3). The uterine glands became deep and tortuous.

A single injection of adequate doses of progesterone thus caused a marked increase in the

value of MI for the epithelium of the uterine wall, uterine glands, and vagina. With an increase in dose from 0.5 to 2.5 mg, no significant change took place in MI. No significant difference was found in the sensitivity of the epithelium of the uterine wall, uterine glands, and vagina to progesterone when given in the above doses. In all groups considerable variations in sensitivity of the mice to progesterone were found (Table 1). Besides the hormone of this particular batch, an experiment was carried out with hormone of batch R-564 (dated November 30, 1964). A single injection of 0.5 mg of this hormone likewise caused a significant increase in MI\*.

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<sup>\*</sup>Hormones of batches 30567 and 10567 (all hormones from the Rostov Factory), in a dose of 0.5 mg, when given as a single injection caused no significant changes in MI.