129. Formation of Deciduomata in Response to Uterine Trauma in Reserpinized Immature Rats with Luteinized Ovaries

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In immature rats with the ovaries mildly luteinized by injections of 5 I.U. PMS and 2 I.U. HCG, uterine traumatization fails to elicit the formation of deciduomata and injections of 10μg estradiol causes vaginal cornification, showing that the induced corpora lutea are not secreting any large amount of progesterone. However, following injections of prolactin (Takewaki, 1969a) or cervical stimulation (Takewaki, 1970), an increased secretion of progesterone takes place in immature animals so primed, as evidenced by the positive deciduomal response to uterine trauma.

Accordingly, it seems likely that the mechanism involved in the regulation of prolactin secretion by the anterior hypophysis is already operative, at least in part, in weanling rats. This conclusion is reinforced by deciduomal response to uterine trauma in immature rats given a single injection of reserpine following pretreatment with 5 I.U. PMS—2 I.U. HCG.

Materials and methods. Three groups of female rats of the T strain were given a single subcutaneous injection of PMS (Primantron, Schering A.G., Berlin) at 21 days of age, followed 50 hours later by a single subcutaneous injection of HCG (Primogonyl, Schering A. G., Berlin). Dose combinations were 5 I.U. PMS and 2 I.U. HCG in Groups 1 and 2 and 40 I.U. PMS and 20 I.U. HCG in Group 3, each dose being dissolved in 0.1 ml of a 0.9% NaCl solution.

Two days after HCG injection, rats of Groups 1 and 3 were given a single subcutaneous injection of 50μg reserpine (Serpasil, Ciba) in 0.05 ml vehicle, while Group 2 animals 5μg reserpine likewise in 0.05 ml solution. All the rats were laparotomized 4 days later under ether anesthesia, and the antimesometrial side of the endometrium was scratched along the entire length of the right uterine horn (Takewaki, 1969a, 1970).

Daily vaginal smears were taken from the day of vaginal canalization until the day before sacrifice performed 4 days after uterine traumatization. Ovaries, and traumatized and intact uterine horns were removed from each rat, trimmed of extraneous tissues and
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weighed. In rats which had received low doses of PMS and HCG (Groups 1 and 2), corpora lutea induced in their ovaries were counted. Uterine horns were examined for gross evidence of deciduomata. Ovaries, uteri and vaginas were fixed in Bouin's solution, sectioned in paraffin and stained with Delafield's hematoxylin and eosin.

All the experiments were carried out at the Zoological Institute, Faculty of Science, University of Tokyo. Rats were kept in an artificially illuminated (14 hours light–10 hours dark), temperature-controlled room.

Results. All the rats were in continued diestrus after reserpine injection throughout the period of vaginal smear examination. Sedation was the obvious symptom in these rats for 1 or 2 days after the injection. In rats which had been given 5 I.U. PMS and 2 I.U. HCG (Groups 1 and 2), ovaries contained 10–28 corpora lutea.

Deciduomal reaction was positive in traumatized uterine horns in 8 of 10 rats of Group 1. However, deciduomata varied considerably in size among different individuals, only 1 of the 8 rats showing full-length reaction. In the rest of the animals, deciduomata were localized to some part or parts of the traumatized horns.

In Group 2 animals which had been injected with 5 \( \mu \)g reserpine after priming with 5 I.U. PMS and 2 I.U. HCG, uterine traumatization invariably failed to elicit formation of deciduomata. Failure of deciduoma formation in response to uterine trauma in immature rats similarly primed with PMS-HCG but not given reserpine has already been reported in the previous paper (Takewaki, 1969a). Group 3 rats which had been primed with 40 I.U. PMS and 20 I.U. HCG prior to reserpine injection were also incapable of reacting to uterine scratching with deciduoma formation. However, traumatized horns were always heavier than the contralateral intact horns in these rats. Vaginae of all groups of rats were mucified. The average ovarian and uterine weights in the 3 groups of animals are given in Table I.

Table I. Average weights in mg(±S.E.) of ovaries and uterine horns in different groups of rats

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of rats</th>
<th>Ovaries</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Traumatized horn</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>34.5±3.7</td>
<td>144.8±14.1</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>29.7±2.1</td>
<td>57.8±7.1</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>113.2±9.1</td>
<td>48.1±1.9</td>
</tr>
</tbody>
</table>

Discussion. It is well established that reserpine initiates prolactin secretion from the anterior hypophysis in adult female rats.
Barraclough and Sawyer (1959) reported that a single injection of 1 mg reserpine per kg body weight on the first day of diestrus was effective in inducing pseudopregnancy in adult rats and this was later confirmed by several workers (Carlson and De Feo, 1965; Carrer and Taleisnik, 1970). Prolactin secretion thus initiated is self-sustaining in the rat probably because progesterone secreted by corpora lutea activated by the prolactin stimulates and maintains further secretion of prolactin by inhibiting the release of prolactin-inhibiting factor (PIF) from the hypothalamus (Rothchild, 1965).

In the present experiments, immature rats received a single injection of 50 μg reserpine 2 days after HCG injection, i.e. on the first day of diestrus in a majority of animals. This dose was approximately equivalent to that used by Barraclough and Sawyer (1959) in adult rats. Since a majority of the reserpinized immature rats which had been primed with 5 I.U. PMS and 2 I.U. HCG formed deciduomata in response to uterine trauma, reserpine appears to be as effective in these immature rats as in adult rats in causing prolactin secretion.

Immature rats similarly primed but not given reserpine (Takewaki, 1969a) and those receiving only 5 μg reserpine following the priming were incapable of developing deciduomata in reaction to uterine traumatization. It is evident, therefore, that a single injection of 50 μg reserpine was responsible for the stimulation of prolactin secretion from the anterior hypophysis.

Thus, in a majority of immature rats which had been pretreated with 5 I.U. PMS and 2 I.U. HCG, uterine traumatization following stimulation of the cervix uteri (Takewaki, 1970) or after injection of 50 μg reserpine resulted in the development of deciduomata. These two lines of evidence indicate that the hypothalamo-hypophysial mechanism involved in the control of prolactin secretion is operating in these rats as in adult animals.

No deciduomata were elicited in response to uterine trauma in immature rats which had received 40 I.U. PMS and 20 I.U. HCG prior to reserpine injection. Immature rats similarly primed also failed to form deciduomata in reaction to uterine trauma applied after mechanical stimulation of the uterine cervix (Takewaki, 1970). In the previous paper, it was reported that immature rats ovariectomized after priming with 40 I.U. PMS and 20 I.U. HCG were totally incapable of reacting to uterine trauma, even if they were placed on a daily injection regimen of 2 mg progesterone and 0.2 μg estradiol, which was highly effective in causing maximal deciduomal growth in traumatized uteri of ovariectomized immature rats having received injections of 5 I.U. PMS and 2 I.U. HCG (Takewaki, 1969b). Accordingly, it is evident that priming with large doses of PMS and
HCG renders the endometrium incapable of responding to trauma even in the presence of optimal combination of progesterone and estradiol in immature animals.

**Summary.** Immature rats which had been primed with 5 I.U. PMS and 2 I.U. HCG were given a single injection of 50 μg reserpine 2 days after HCG. A majority of the animals exhibited positive deciduomal reaction following uterine traumatization performed 4 days after reserpine injection. This finding together with the writer's previous report that immature rats similarly primed develop deciduomata in response to uterine trauma applied after cervico-vaginal stimulation (Takewaki, 1970) indicates that the hypothalamic mechanism involved in the regulation of hypophysial prolactin secretion is operative, at least in part, in immature rats.

Those animals which had been pretreated with 40 I.U. PMS and 20 I.U. HCG failed to form deciduomata in reaction to uterine trauma given after injection of 50 μg reserpine. This is in harmony with the previous report that the endometrium is incapable of responding to trauma in such animals even in the presence of optimal combination of progesterone and estradiol supportive of deciduomal growth (Takewaki, 1969b).

**References**
