OVARIAN STIMULATION BY OESTROGENS

2. STIMULATION IN THE ABSENCE OF HYPOPHYSIS, UTERUS, AND ADRENAL GLANDS

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It has been suggested in discussion that the ovarian stimulation produced by oestrogen in the hypophysectomized immature rat [Williams, 1940, 1944; Pencharz, 1940] may be an indirect effect mediated through the adrenals or uterus. Bourne & Zuckerman [1942 a, b] have demonstrated that the adrenals play an important part in the regulation of the oestrous cycle in the rat, while the observation of Palmer & Fulton [1941] that the response to chorionic gonadotrophin is diminished in the absence of the uterus indicates that this organ may also be concerned in ovarian stimulation. The following experiments show that the adrenals and the uterus are not involved in the stimulation of the ovary by oestrogens.

STIMULATION IN THE ABSENCE OF HYPOPHYSIS AND UTERUS

Method

A group of immature female rats was hysterectomized. A week later some were killed and the remainder hypophysectomized. Of the hypophysectomized rats, some were injected daily with 100 µg. of stilboestrol dissolved in 0.2 ml. of sesame oil. All the rats were killed 5 days after hypophysectomy. The ovaries were dissected and weighed after fixation in Bouin's fluid and transference to 70% alcohol and subsequently cut in serial section and stained with haematoxylin and eosin.

Five days after hypophysectomy the ovaries are significantly lighter than normal, but their normal weight is maintained or increased by a daily injection of 100 µg. of stilboestrol [Williams, 1944].

Table 1

<table>
<thead>
<tr>
<th>Organs removed</th>
<th>Daily stilboestrol injection µg.</th>
<th>No. of rats</th>
<th>Wt. of organs mg. ± m</th>
<th>Significance of difference from control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>0</td>
<td>5</td>
<td>8.3±0.9</td>
<td>—</td>
</tr>
<tr>
<td>Uterus</td>
<td>0</td>
<td>5</td>
<td>10.0±1.3</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>10</td>
<td></td>
<td>9.2±0.8</td>
<td>—</td>
</tr>
<tr>
<td>Exp. 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysis</td>
<td>0</td>
<td>5</td>
<td>5.7±0.6</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Uterus</td>
<td>100</td>
<td>9</td>
<td>13.3±1.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Exp. 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophysis</td>
<td>100</td>
<td>7</td>
<td>9.7±0.7</td>
<td>ca. 0.7</td>
</tr>
<tr>
<td>Uterus</td>
<td>ca. 1000†</td>
<td>5</td>
<td>10.4±1.0</td>
<td>ca. 0.4</td>
</tr>
</tbody>
</table>

† Dosage explained in text.

Results

The results in different groups are recorded in Table 1 and show that hysterectomy alone affects neither the weight of the ovaries nor the fall that normally occurs after

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hypophysectomy, and that the stilboestrol-injected rats have ovaries significantly heavier than have normal rats.

Histologically the ovaries of the stilboestrol-injected rats were indistinguishable from those of hypophysectomized rats with intact uteri given the same treatment. The number of follicles more than 200µ in diameter was obviously increased, and the majority of these follicles had no antra.

STIMULATION IN THE ABSENCE OF THE HYPOPHYSIS, UTERUS, AND ADRENALS

Method

A group of immature female rats was hypophysectomized and adrenalectomized 5 days after their uteri had been removed. Their drinking water was replaced by physiological saline. Half of them were injected subcutaneously with 100µg. of stilboestrol in 0.2 ml. of sesame oil on the day of hypophysectomy and on the 4 succeeding days. All the rats were killed 5 days after hypophysectomy and their ovaries treated as in the previous experiment.

Results

In error, an overstrong solution of stilboestrol was prepared and the rats in one group in the Table were injected with 1000µg. daily in two cases, and for the first of the five injections in the case of the other three rats. The rats in the other group were given the proper dose of 100µg. daily.

The results give no indication that adrenalectomy had interfered with the ovarian stimulation. When the ovarian sections were examined microscopically it was found that several ovaries in both the control and injected groups were completely atrophic, all the ovarian tissue being replaced by connective tissue stroma. This is attributed to interference with the blood supply during hysterectomy and would account for the failure of the stilboestrol injections to increase the normal ovarian weight as they did in the previous experiment. The other ovaries, however, showed a normal atrophy in the control group and stimulation in the injected groups exactly as if the uterus and adrenals had been present.

SUMMARY

The ovarian stimulation produced by stilboestrol injections in immature hypophysectomized rats is unaffected by removal of the uterus, or of the uterus and adrenal glands.

There is no evidence that this effect of oestrogens is an indirect one.

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REFERENCES