EFFECT OF ESTRADIOL, ESTRONE, AND ESTRIOL ON RNA BIOSYNTHESIS IN THE RAT UTERUS AT VARIOUS TIMES AFTER OVARIECTOMY

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The action of estradiol, estrone, and estriol on the biosynthesis of high-polymer RNA in the uterus of ovariectomized rats was investigated. The action of the estrogens on RNA biosynthesis was found to depend on the chemical structure of the hormone and on the time elapsing after ovariectomy.

The stimulating action of estrogens on RNA biosynthesis in cells of the uterus has often been described [1, 2, 4]. Meanwhile, no comparative analysis of the effects of estradiol, estrone, and estriol on RNA biosynthesis in the uterus at different times after ovariectomy has yet been carried out.

This paper describes a differential study of the effect of ovariectomy and a single injection of estrogens on the biosynthesis of high-polymer RNA.

EXPERIMENTAL METHOD

Altogether 450 noninbred female albino rats weighing 150-180 g were used. The animals were ovariectomized through a dorsal incision under superficial ether anesthesia and sacrificed on the 3rd, 7th, 14th, and 21st days after the operation. The experimental rats received a single intraperitoneal injection of estradiol, estrone, or estriol in doses of 10 and 25 mg/100 g body weight, dissolved in 1% ethanol, 4 h

TABLE 1. Effect of Ovariectomy and Estrogens on RNA Biosynthesis in the Rat Uterus (M ± m)

Hormone	Dose, μg/100 g	Incorporation of P^{32} into RNA of uterus of ovariectomized rats (pulses/min/mg RNA) at different times after ovariectomy			
		3rd day	7th day	14th day	21st day
Control	—	1254±63	943±59	730±22	652±30
Estradiol	10	4278±205*	3540±143**	2414±102	2838±126
	25	3215±274	2642±163	2358±163	2462±149
Estrone	10	3311±311	2578±140	2871±267	2664±368
	25	3423±101	3117±280	2274±238	2439±216
Estriol	10	3206±369	2673±189	2341±267	2203±206
	25	3128±366	2546±281	2371±226	2538±243

Note. All results obtained after administration of estrogens are statistically significant relative to the control. One asterisk denoted a result significant relative to the effect of estrone and estriol, two asterisks a result significant relative to the effect of estriol ($P < 0.05$). Radioactivity of RNA (pulses/min/mg) 1070 ± 112 in diestrus and 4445 ± 342 in estrus.

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TABLE 2. Effect of Ovariectomy and Estrogens in a Dose of 10 μg/100 g on Weight of Rats' Uterus (M ± m)

Day after ovariectomy	Weight of uterus (mg)			
	control*	estradiol	estrone	estriol
3 rd	420±30	489±19	462±31	429±14
7 th	356±42	421±32	393±51	385±27
14 th	218±27	267±34	313±27	238±38
21 st	83±21	220±15	192±50	207±33

*Weight of uterus 338 ± 28 mg in diestrus and 495 ± 32 mg in estrus.

before sacrifice. Control animals received an equal volume of the solvent. Disodium hydrogen phosphate-P^{32}, diluted in physiological saline, was used as the labeled precursor of RNA and injected intraperitoneally in a dose of 0.5 μCi/g body weight 1 h before sacrifice. The uterus was removed, freed from connective tissue, and all subsequent procedures were carried out at 4°C. Each sample consisted of the uteri of three ovariectomized rats. The high-polymer fraction of RNA was isolated by the phenolic method of Sherrer and Darnell [5] with certain modifications. For further deproteinization the preparations were treated with chloroform, and to separate the high-polymer RNA, salt fractionation with a 2.5 M sodium chloride solution was used. The RNA content was determined with the SF-4A spectrophotometer. Activity of the samples was counted with the NAG-β M gas-flow counter.

EXPERIMENTAL RESULTS

The experiments show that as a result of ovariectomy the weight of the uterus decreased and biosynthesis of RNA in its cells was reduced. On the third day after the operation the level of RNA synthesis was rather higher than later during the investigation. On the 7th, 14th, and 21st days the weight of the uterus and the rate of RNA biosynthesis in the endometrial cells of the ovariectomized animals decreased progressively (Tables 1 and 2).

A single injection of estradiol, estrone, and estriol was accompanied by a marked increase in the wet weight of the uterus and in RNA synthesis. Characteristically the most significant effects in every case were found on the third day after ovariectomy. At that time maximal stimulation of RNA biosynthesis was discovered after injection of estradiol in a dose of 10 μg/100 g body weight, when the level of incorporation of the labeled precursor was 341% of the control. Increasing the dose of hormone to 25 μg/100 g reduced the effect somewhat. During this period the rate of incorporation of the label also was high after injection of estrone and estriol, but it did not change by a statistically significant amount after injection of larger or smaller doses of the hormone.

On the fourteenth day after ovariectomy estradiol in a dose of 10 μg/100 g also greatly accelerated the incorporation of P^{32} into high-polymer RNA in the uterus. The weight of the uterus showed a smaller change. A relatively high level of radioactivity of the RNA in this series of experiments also was found after injection of estrone in a dose of 25 μg/100 g (Table 1).

All the estrogens studied, when injected on the 14th and 21st days after ovariectomy, increased the weight of the uterus and accelerated RNA synthesis equally. No statistically significant differences between the action of these steroids at these times depending on their chemical structure or the dose used were found.

The experiments thus showed that involution of the uterus and a progressive decrease in RNA synthesis take place as a result of ovariectomy. In addition, during the experimental period the sensitivity of the cells to injected estrogens varies, as reflected by a decrease in the rate of RNA biosynthesis and the disappearance of differences between the action of the individual hormones. The results show that in the early period after ovariectomy (on the third day) RNA synthesis was increased by a greater degree after injection of estradiol. An increase in the dose of that hormone led to a decrease in the incorporation of label into RNA. This result is in agreement with others obtained previously [3] when a decrease in the RNA-polymerase activity was discovered after an increase in the dose of estradiol, starting from 10 μg. In the later periods after ovariectomy stimulation of RNA biosynthesis by estrogens was less marked, and this evidently indicates a more severe disturbance of the functional activity of the target cells for the estrogens.

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