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RESPONSE OF THE INFANTILE RAT OVARY TO INTRASPLENIC TRANSPLANTATION INTO ADULT CASTRATED DIABETIC ANIMALS

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In rats with experimental diabetes, compensatory hypertrophy of the ovary is weak or may be absent altogether [2]. It has been suggested that the response of the pituitary to a fall in the blood estrogen level is depressed in diabetes [2]. It was decided to study how the pituitary of diabetic rats responds to a sharper decline in the estrogen level, caused by transplantation of the ovaries into the spleen. Such transplantation is known to lead to inactivation of most of the estrogen produced by the ovary in the liver, and in turn this leads to increased secretion of gonadotrophins and to hypertrophy of the transplanted ovaries [1, 4]. The investigation described below was undertaken to study this problem.

EXPERIMENTAL METHOD

Adult female albino rats weighing on average 246 ± 4 g were castrated under pentobarbital anesthesia, after which one ovary, taken from an infantile animal, was implanted into their spleen. The weight of this ovary was 4-10 mg. All the animals 7-9 days after plantation, when survival of the graft could be expected, were divided into two groups. One group served as the control; animals of the other group received a subcutaneous injection of freshly prepared alloxan in a dose of 16 mg/kg. Vaginal smears were taken from all the rats, and in those receiving alloxan the diuresis and sugar concentration in the urine were studied. Rats with marked diabetes and control animals were decapitated 33 days after the injection of alloxan. The blood sugar of these animals was determined by the picrate method. The ovary was removed from the spleen and weighed. The uterus, pituitary, adrenals, and vagina also were weighed. The uterus and transplanted ovary were fixed in Bouin's fluid for histological treatment. The height of the uterine epithelium, epithelium of the uterine glands, and diameter of the follicles were measured. Only those animals with no adhesions between the spleen and peritoneum were taken into consideration. In addition, the total gonadotrophin level in the pituitary was determined in infantile cocks of the White Russian breed. Each cock received subcutaneous injections of saline extracts of pituitary glands twice a day for 5 days in a total dose of 8 mg. The degree of response was judged from the change in weight of the testes and comb.

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TABLE 1. Effect of Alloxan Diabetes on Degree of Hypertrophy of Ovary Transplanted into Spleen of Castrated Rats

Character of experiment	Number of animals	Final body weight, g	Blood sugar, mg/100 ml	Sugar in urine, %	Weight of transplanted ovary, mg/100 g body weight	Weight of pituitary, mg/100 g body weight	Weight of adrenals, mg/100 g body weight
Control	21	267±7	69,8±3,6	—	64,2±12,4	12,4±0,63	56,3±1,2
Alloxan	15	209±7	459±33,6	9,4±1,7	31,9±6,8 $P<0,05$	8,2±0,4 $P<0,001$	54,3±2,2

Note. After castration ovary of an infantile rat was transplanted into spleen of these rats.

EXPERIMENTAL RESULTS

In the course of the experiments 33% of rats receiving alloxan died. The surviving animals had well-marked diabetes (Table 1). The average weight of the transplanted ovary in the group of diabetic rats was less than in the group of control animals, in agreement with data showing a decrease in compensatory hypertrophy of the ovary in diabetes. The weight of the pituitary also was less in the diabetic rats than in the controls. There were no differences in weight of the adrenals in the groups. The vaginal smears of all diabetic rats remained characteristic of diestrus throughout the experiment. The height of the endometrial epithelium was very low, namely 11.51 ± 0.7 μ, much less than the height of the epithelium in intact animals (24.4 ± 2 μ). Considering that the reactivity of diabetic rats to estrogen is in any event not lower, but rather even higher than the reactivity of normal animals [3], this low height of the uterine epithelium observed in diabetic rats in the present experiments and the diestrus type of vaginal smear must be regarded as indications of estrogen deficiency. In 62% of rats of the control group the vaginal smears also were of the diestrus type. The height of the uterine epithelium in these animals was low (11.2 ± 0.6 μ). However, persistent estrus was found in 38% of the control animals. The weight of the uterus in these rats was increased by 134%, and of the vagina by 60%, while the height of the endometrial epithelium was 38% greater than in the remaining animals. All these facts indicated that part of the estrogen secreted by the ovary in these rats escaped inactivation in the liver.

The content of total gonadotrophins in the pituitary glands of the diabetic and control animals was identical.

Histological analysis of the ovaries showed proliferation of connective tissue and tissue of the granulosa-cell type in the hypertrophied ovaries of 71.5% of the control animals with persistent diestrus. Follicles were completely absent. In the group of diabetic rats, this structure was found in only 15% of individual animals, but it was not found at all in the control rats with persistent estrus. Follicles of different sizes, some of them very large (up to 1000 μ), and corpora lutea were present in the grafts in animals with persistent estrus. In most diabetic animals the same components were observed in the hypertrophied ovaries but corpora lutea predominated.

Considerable disturbances of ovarian structure were thus found in most rats in the group of control animals with persistent diestrus. Why is this so? The following explanation can be offered. In most control rats with permanent diestrus, estradiol evidently did not penetrate into the blood, as is shown not only by the character of the vaginal smears, but also by the low height of the uterine epithelium. Under these conditions the pituitary secreted large quantities of gonadotrophins, which induced prolonged and excessive stimulation of the ovaries, disturbing their structure. In control rats with persistent estrus, since some estrogen escaped inactivation in the liver, secretion of gonadotrophins was moderate, and there was no excessive stimulation of the ovaries grafted into the spleen. In diabetic rats, despite estrogen deficiency, secretion of gonadotrophins also was averaged, evidently because of the depressed response of the pituitary to a fall in the blood estrogen level. Consequently, in this group also, these grafts in most animals were not exposed to increased stimulation.

The data given above on the character of response of ovaries transplanted into the spleen of diabetic rats suggest that the view expressed by the writers previously, that the response of the pituitary to a fall in the blood estrogen level is weakened in diabetes, is confirmed.

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