

FUNCTIONAL MORPHOLOGY OF THE UTERINE CAPILLARY BED AFTER INJECTION OF DIHYDROSTILBESTROL

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Dihydrostilbestrol and other preparations stimulating estrogen production are frequently used in clinical practice for the treatment of diseases of the female reproductive system. There is reason to suppose that an estrogen, which acts directly on the smooth myocytes of precapillary sphincters, helps to improve the blood supply to the uterus [8, 9]. Meanwhile reports have been published in recent years of the unfavorable aftereffects of long-term use of such preparations for the reproductive organs and, in particular, for the uterus [2-4]. Menorrhagia, dysmenorrhea, pericapillaritis, fibrosis, and sclerotic changes in the stroma of these organs have been observed in women.

The aim of this investigation was to study the structure of the capillary bed of the rat uterus in the recovery period after repeated injections of dihydrostilbestrol.

EXPERIMENTAL METHOD

The uterus of sexually mature noninbred albino rats weighing 180-200 g was studied. Two groups of animals (20 rats in each group) served as the control: 1) intact animals, 2) animals receiving 0.2 ml of physiological saline daily for 7 days intramuscularly. The experiments were carried out on 48 rats, which received daily injections of 0.2% solution of dihydrostilbestrol, in a dose of 2 mg/kg body weight per mouse, for 7 days. The animals were killed by decapitation on the 1st, 3rd, 5th, 10th, 30th, and 60th days after the last injection of dihydrostilbestrol. Frozen sections 25 μ thick were mounted on coverslips, dried for 15-20 min, and stained by the method of Koenig and Vial [6] for detecting magnesium-dependent adenosine triphosphatase (Mg-ATPase) in the capillary walls. Morphometric parameters of the capillary bed adopted in histochemical investigations [5] were studied in three fields of vision, separately in each of six sections, and individually for each animal. The data were subjected to statistical analysis [1].

EXPERIMENTAL RESULTS

In animals of both control groups the uterine capillaries were revealed in the form of bands with very clear outlines (Fig. 1a). In most cases they were straight, but sometimes gentle curves and small projections were visible along their course. Injection of dihydrostilbestrol caused considerable structural changes in the uterine capillary bed (Fig. 1, b-d). As Fig. 1 shows, the more marked transformations of the microcirculatory bed were observed in the endometrium. Not less than 20 days after termination of the injection of dihydrostilbestrol, numerous twisted vessels could be seen, forming anastomoses and dense plexuses with one another. Particularly important structural changes in the microcirculatory bed, however, were observed during the first 5 days of the recovery period (Fig. 1b). During this period the highest values of enzyme activity were obtained ($p < 0.001$) in the capillary walls (Fig. 2a). Most vessels were stained brown or dark brown, evidence of a high intensity of the course of the histochemical reaction in their wall. The total length of the capillaries also was significantly greater ($p < 0.01$) than the control values, but only in the endometrium.

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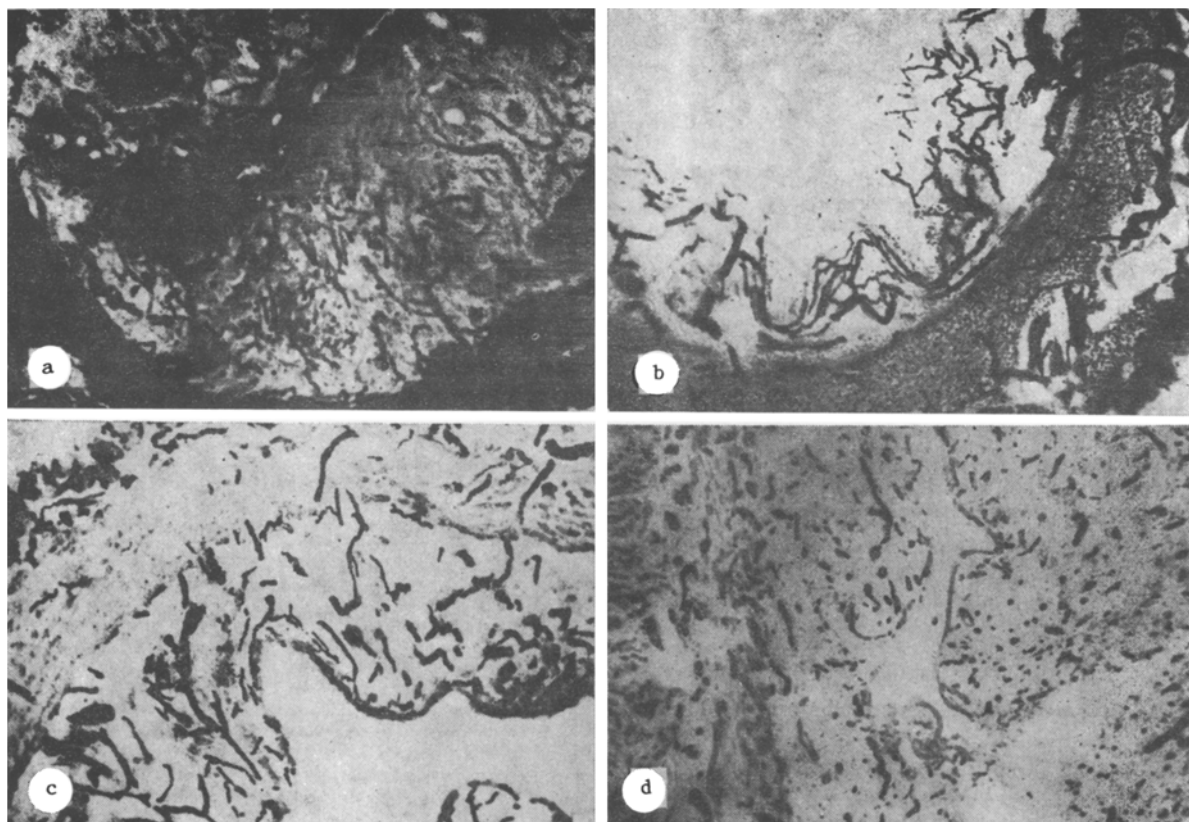


Fig. 1. Changes in microcirculatory bed of rat uterus during recovery period after injections of dihydrostilbestrol. a) Control, b) 5th day of experiment; c) 20th day of experiment; d) 30th day of experiment. Method of Koenig and Vial. 42 \times .

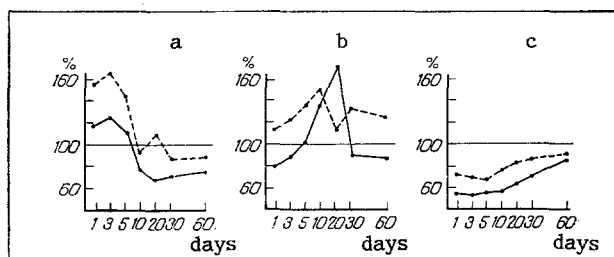


Fig. 2. Parameters of active enzyme (a), and total length (b) and mean diameter (c) of capillary bed of rat uterus during recovery period after injections of dihydrostilbestrol. Continuous line - myometrium; broken line - endometrium. Values of parameters in uterine capillaries of control animals taken as 100%.

In the myometrium the density of these vessels during the first 3 days of the recovery period remained quite low (78-85% of the initial level; $p < 0.01$), and only on the 5th day, having started to rise again, did they reach the values established in the control animals ($p > 0.05$; Fig. 2b). A decrease in the diameter of the capillaries was present to a greater degree in the myometrium than in the endometrium (Fig. 2c).

Between the 5th and 20th days of the recovery period capillaries with low and moderate enzyme activity were found increasingly often in the uterus. The mean values of the parameter therefore were reduced, but they fell significantly ($p < 0.01$) below the control level only in the myometrium on the 10th day (Fig. 2a). On the 20th day after the last injection of dihydrostilbestrol the lowest values of enzyme activity ($p < 0.001$) were observed in capillaries of the myometrium, but the highest values were obtained for the total length of these vessels ($p < 0.05$; Fig. 2b). The largest number of capillaries with low enzyme activity in the

endometrium was observed on the 30th day of the recovery period (Fig. 1d). The mean value of the optical density of the precipitate in the endometrial microvessels became significantly lower than values obtained in the control animals ($p < 0.05$). The total length of the capillaries and their mean diameter in the uterine mucosa, on the other hand, increased (Fig. 2b, c). Many profiles of capillaries could be seen in the endometrium of the experimental animals studied at this period (Fig. 1d). The value of all the parameters characterizing the state of the capillary bed in the myometrium remained significantly below ($p < 0.01$) the control values (Fig. 2).

During the next 30 days of the recovery period, values of enzyme activity and total length of the capillaries, although they approached the control level, with the exception of the mean diameter of these vessels, they still differed significantly ($p < 0.05-0.01$) from it (Fig. 2).

Repeated injections of dihydrostilbestrol, stimulating estrogen production [7], thus induce appreciable qualitative and quantitative changes in the microcirculatory bed of the uterus, which last at least 2 months after the final injection of the hormone.

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