

# FUNCTIONAL MORPHOLOGY OF THE UTERINE CAPILLARY BED AFTER ADMINISTRATION OF DIETHYLSTILBESTROL

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Hexestrol and other preparations stimulating estrogen production are frequently used in clinical practice for treatment of diseases of the female reproductive system. There is reason to suppose that estrogens, with a direct action on smooth myocytes of precapillary spinclers, with a direct action of these preparations on the vascular bed of the reproductive organs and, in particular, of the uterus have been published recently [2-4]. Menorrhagia, dysmenorrhea, pericapillaritis, fibrosis, and sclerotic changes in the stroma of these organs have been described in women.

The aim of this investigation was to study the structure of the capillary bed of the rat uterus after administration of hexestrol.

## EXPERIMENTAL METHOD

Experiments were carried out on the uterus of sexually mature noninbred albino rats weighing 180-200 g. Two groups of animals (20 rats in each group) were used as the control. Group 1) intact animals, Group 2) animals receiving 0.2 ml physiological saline daily for 7 days by intramuscular injection. The experiments were carried out on 49 rats, receiving 0.22 hexestrol solution daily for 7 days (at the rate of 2 mg/kg body weight, intramuscularly). The animals were killed by decapitation on the 1st, 3rd, 5th, 10th, 20th, 30th, and 60th days after the last injection of the hormone. Frozen sections 25  $\mu$  thick were mounted on coverslips, dried for 15-20 min, and stained by the method in [6] to reveal Mg-ATPase in the capillary walls. Morphometric parameters of the capillary bed, as adopted for histochemical investigations [5], were studied in three fields of vision, in each of six sections separately, and for each animal individually. The numerical data were subjected to statistical analysis [1].

## EXPERIMENTAL RESULTS

In animals of both control groups, uterine capillaries were visible as bands with very clear outlines (Fig. 1a). In most cases they were straight, and sometimes gentle curves and small projections were visible along their course. Administration of hexestrol caused considerable structural changes in the uterine capillary bed (Fig. 1b-d). More marked transformations of the microcirculatory bed were observed in the endometrium. Not less than 20 days after termination of the injections of hexestrol multiple twisted vessels, anastomosing with one another to form dense plexuses, were observed here. Particularly significant structural changes in the microcirculatory bed, however, were observed in the first 5 days of the recovery period (Fig. 1b). During this period the highest values were obtained for activity of the enzyme ( $p < 0.001$ ) in the capillary walls (Fig. 2a). Most vessels were stained brown or dark brown, evidence of the high intensity of the course of the histochemical reaction in their walls. The total length of the capillaries also was significantly higher ( $p < 0.01$ ) than the control values, but only in the endometrium. In the myometrium the density of these vessels was quite low during the first 3 days of the recovery period (78-85% of the initial level,  $p < 0.01$ ), and not until the 5th day did it rise to reach the values established in the control animals ( $p < 0.05$ , Fig. 2b). The diameter of the capillaries was reduced by a greater degree in the myometrium than in the endometrium (Fig. 2c).

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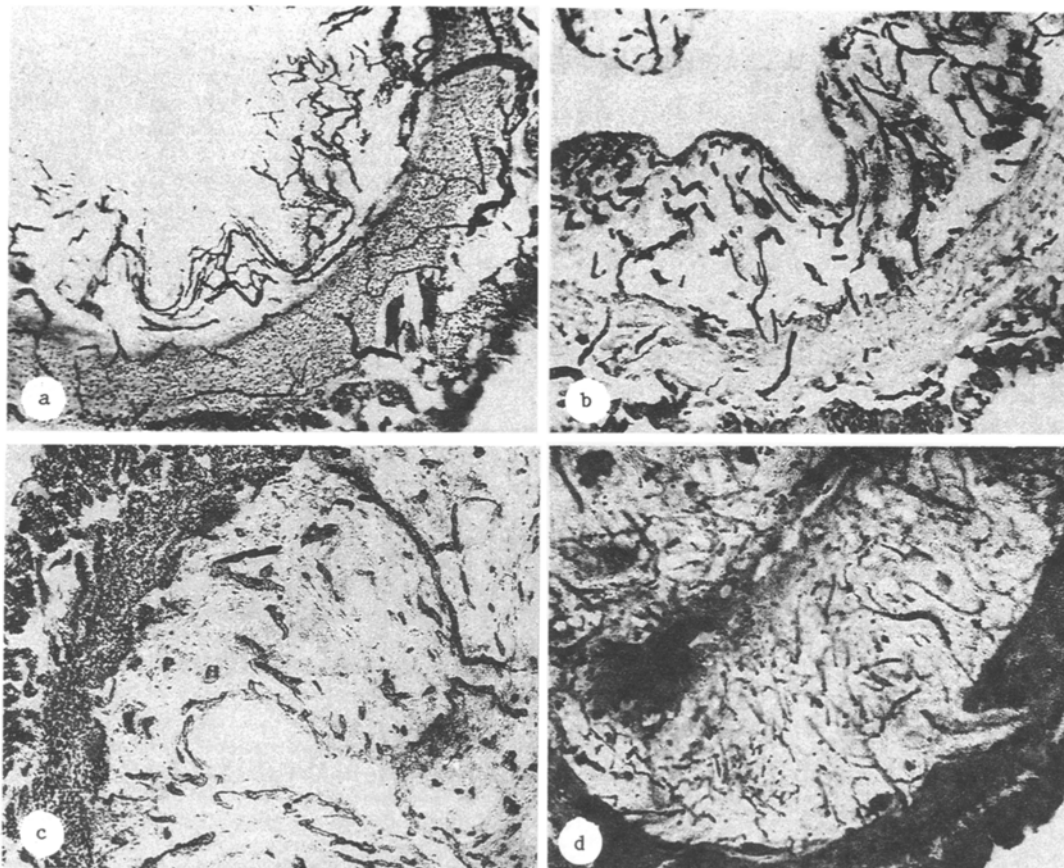


Fig. 1. Changes in microcirculatory bed of rat uterus during recovery period after injection of hexestrol. a) Control; b, c, d) 5, 20, and 30 days of experiment respectively. Objective 6.3, ocular 7.

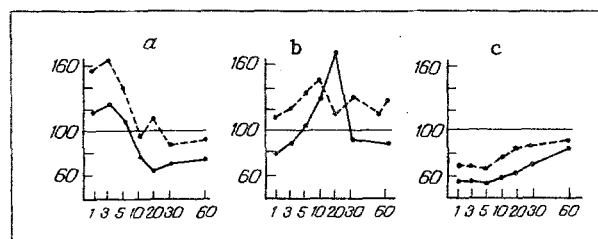


Fig. 2. Parameters of enzyme activity (a), and total length (b) and mean diameter (c) of capillary bed of rat uterus during recovery period after injection of hexestrol. Abscissa: days after last injection of hormone. Broken line — endometrium, continuous line — myometrium. Value of parameters in uterine capillaries of control animals taken as 100%.

Between the 5th and 20th days of the recovery period capillaries with low and average enzyme activity were observed increasingly often in the uterus. The mean values of the parameter therefore decreased, but only in the myometrium and on the 10th day did they fall significantly ( $p < 0.01$ ) below the control level (Fig. 2a). On the 20th day after the last injection of the hormone, the lowest values of enzyme activity ( $p < 0.001$ ) were observed in the 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 optical density of the precipitate in the microvessels of the endometrium became significantly lower than values recorded in the control animals ( $p < 0.05$ ). The total length of the capillaries and their mean diameter in the uterine mucous membrane, on the other hand, were

increased (Fig. 2b, c). In the myometrium, the value of all parameters studied characterizing the state of the capillary bed remained significantly below ( $p < 0.01$ ) the control values (Fig. 2a-c).

During the next 30 days of the recovery period values of enzyme activity and total length or diameter of the capillaries, while close to the control level, still differed significantly from it, if the mean diameters of these vessels are excluded (Fig. 2a-c;  $p < 0.05-0.01$ ).

Repeated injections of hexestrol, stimulating estrogen production, thus caused appreciable qualitative and quantitative changes in the microcirculatory bed of the uterus, which continued for at least 2 months after the last injection of the hormone.

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