

# EFFECT OF ESTROGEN ON THE ADRENERGIC NERVOUS APPARATUS OF THE RAT UTERUS

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Adrenergic nerve fibers were detected in the myometrium of a rat in the stage of diestrus by means of an aqueous formaldehyde histochemical method for catecholamines. Most fibers are connected with blood vessels while the rest lie freely in the myometrium. Injection of estrogen into the rats 48 h before removal of the tissue causes a marked increase in the number of detectable adrenergic nerve fibers supplying the myometrium but has virtually no effect on the number of fibers lying around the vessels.

The rat myometrium is one of the most intensively studied objects in connection with the physiology of smooth muscles. The motor response of these muscles to catecholamines depends substantially on the estrogen level in the body [8]. Until recently it was not clear whether the rat myometrium receives an adrenergic innervation or whether changes in the reactivity of the muscle are accompanied by changes in the expressiveness of the adrenergic innervation. By means of a gaseous formaldehyde method for histochemical detection of catecholamines Sjöberg [7] showed the presence of adrenergic fibers weaving among the blood vessels and innervating the muscle of the uterus of certain mammals; however, like Norberg and Fredricsson [5], he denied the existence of extravascular fibers in the rat uterus. More recent investigations have shown a limited adrenergic innervation of the muscle, chiefly in the region of the cervix uteri [3, 4].

This paper describes a comparative investigation of the adrenergic innervation of the rat myometrium during diestrus, when the estrogen level is low, and when the level of the hormone is artificially raised.

## EXPERIMENTAL METHOD

The control group consists of five sexually mature female albino rats in the stage of diestrus. In the main group, 48 h before removal of the tissue, five sexually mature female albino rats received an injection of 1000  $\mu$ g 17- $\beta$ -estradiol benzoate in 1 ml peach oil. All the rats had a normal 4-day estrous cycle. The stages of the cycle were determined by vaginal smears in the usual way [2].

Histological specimens were prepared from an area in the middle of the uterine cornu. Luminescence of catecholamines was obtained by using the aqueous formaldehyde method of Sakharova and Sakharov [1]. The procedure was as follows. Pieces of tissue were incubated for 45 min on ice in 4% formalin solution made up in physiological saline, after which the tissue was frozen with carbon dioxide and cut into sections on a cryostat at  $-15^{\circ}\text{C}$ . The sections, mounted on a slide, were dried for 18-20 h under  $\text{P}_2\text{O}_5$  and placed in mineral oil. The sections were then heated to  $80^{\circ}\text{C}$  for 10-12 min and examined and photographed in the ML-2 luminescence microscope.

## EXPERIMENTAL RESULTS

By use of this method noradrenalin of the sympathetic nerve fibers is revealed. These fibers were found in all specimens of both the experimental and the control series.

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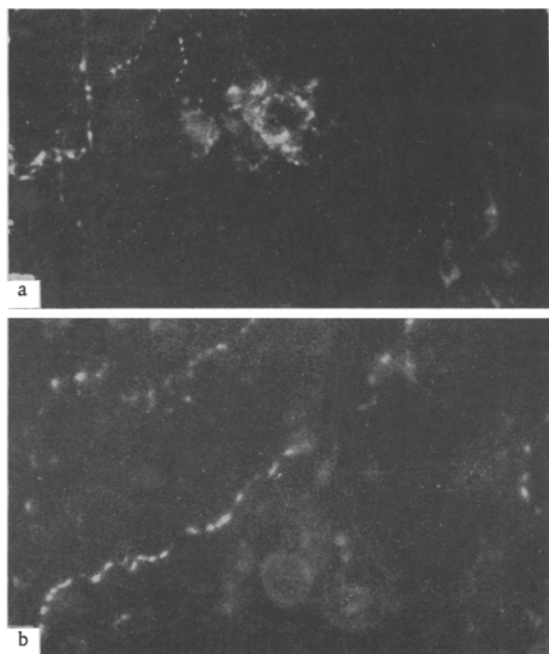


Fig. 1

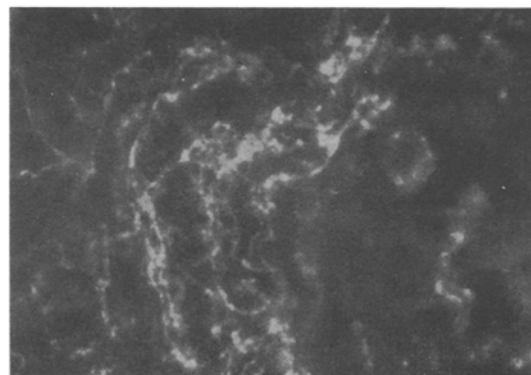


Fig. 2

Fig. 1. Adrenergic nerve fibers in myometrium of rat in state of diestrus. Single varicose nerve fibers lying freely in the myometrium can be seen: a) blood vessel surrounded by plexus of adrenergic fibers; b) blood vessels with no surrounding halo of detectable fibers, 400  $\times$ .

Fig. 2. Adrenergic nerve fibers from animal treated with estrogen. Extensive nerve plexuses formed by thin fibers and located chiefly actually in the myometrium have appeared, 400  $\times$ .

Nerve fibers were most numerous on the surface of the uterine cornu, in the perimetrium. Many adrenergic nerve fibers were contained in perivascular plexuses surrounding the blood vessel. However, in the myometrium of the uterus of the control rats there were many free adrenergic fibers unconnected with the blood vessels (Fig. 1).

In the rats receiving estrogen the number of nerve fibers in the myometrium was considerably increased and, besides the free-lying adrenergic fibers observed in the control series, there were also massive nerve plexuses formed by thin nerve fibers (Fig. 2). In some control preparations stained by Van Gieson's method extravascular nerve fibers and plexuses were in fact observed in areas of the preparations free from blood vessels.

The character of the adrenergic innervation in the perimetrium of the experimental animals was indistinguishable from that in the control. Treatment with estrogen had no appreciable effect likewise on the number of fibers connected with the blood vessels.

These results show that the adrenergic nervous apparatus in the rat uterus is more highly developed than was hitherto considered. According to Norberg and Fredricsson [5], the uterus receives its sympathetic innervation mainly in the region of the tubo-uterine junction, while Kanerva et al. consider that the cervix uteri receives the most highly developed innervation. The present investigation showed a well-developed sympathetic innervation in the uterine cornu, an area remote both from the cervix and the tubo-uterine junction. A definite increase in the number of extravascular adrenergic fibers detected in the myometrium of rats receiving estrogen corresponds to results obtained for the rabbit uterus [7]. It is postulated that the adrenergic fibers innervating the myometrium arise from short adrenergic neurons [6] whose bodies lie in Frankenhauser's ganglion [4]. It has not yet been settled whether estrogens act directly on the cells of this ganglion or whether the increase in the number of nerve fibers containing noradrenalin observed is the result of tissue interactions in the course of the response of the myometrium and endometrium to the estrogen.

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