

INTERACTION OF PROGESTERONE AND ESTROGENS  
ON THE HYPOTHALAMIC CENTER CONTROLLING  
ESTROUS BEHAVIOR IN SHEEP

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**Abstract.** Behavioral estrus of castrated and with progesterone treated ewes, induced by implantation of  $17\beta$ -estradiol into the area controlling the sexual behavior, was completely modified as compared with that of castrated but non treated with progesterone ones. The length of behavioral estrus in the non treated ewes was 24-30 hr and its symptoms were rather weakly expressed. On the contrary, the ewes treated with progesterone did not exhibit any behavioral estrus after implantation throughout the whole period of the treatment. They showed symptoms of behavioral estrus on the 2nd day after the injections of progesterone were stopped; in such cases the symptoms were strongly expressed and lasted for 3-6 days. Since the estradiol, implanted into the hypothalamic sexual behavior center, was acting locally, the described reaction of ewes might be thought of as the effect of interaction of progesterone and estradiol being displayed on the level of specific neuronal receptors of this center.

INTRODUCTION

It has been found in our previous experiments (1) that the anterior region of the medial basal hypothalamus (MBH) in sheep takes part in the control over the estrous behavior and most probably over liberation of gonadotrophin releasing factors. These findings raised the question whether the site for estrogen inhibitory feedback receptor is also localized in this region. Unexpected results obtained in the preliminary investigations on this problem suggested an idea of interaction of progesterone and estrogens in the influence on the hypothalamic center controlling estrous behavior in sheep. In the present work the main attention has been paid to this phenomenon.

In the above mentioned preliminary investigations on the existence of an inhibitory feedback receptor in the MBH of sheep following results

were obtained. All the cycling ewes (six) with locally acting estrogen implanted into the anterior region of MBH on 6-10 days of estrous cycle showed ovulations at the next and subsequent physiological terms of the estrous cycles. Although none of the implanted ewes exhibited any symptoms of estrous behavior on the days which immediately followed the implantation, they did exhibit this behavior on days of their physiological estrous terms, that means on 17th or 18th day of the estrous cycle. However, the course and character of estrous behavior in the implanted ewes were modified. Duration of estrous period in these animals was markedly prolonged to 3-6 days (instead 24-36 hr as in physiological cycles) and the symptoms of this behavior were more strongly expressed. The lack of the estrous behavior response to the estradiol implantations in cycling ewes in the middle of the estrous cycle became the subject of consideration and raised the suggestion that progesterone secreted by cyclic corpus luteum might suppress the action of implanted estradiol on the neurons of this center. The experiments to be described were undertaken to prove this suggestion.

#### MATERIALS AND METHODS

The experiments were carried out on 12 castrated Merino ewes. Nine out of them were given intramuscularly 10 mg of progesterone per day, 2 days before estradiol implantation and on 1st, 2nd or 4th subsequent day following implantation. The remaining animals acted as controls.

*Implantation of 17- $\beta$ -estradiol.* 17- $\beta$ -estradiol was implanted in the tubings, containing it in a melted form only in their barrels. The hormone in this form acting locally on the neurons surrounding the site of the hormone implantation elicited behavioral estrus in castrated ewes (1). The implantation of the hormone into the anterior region of MBH was carried out bilaterally by means of stereotaxic technique described by Traczyk and Przekop (5).

Behavioral estrus was determined by running the implanted ewes with the ram.

At the end of the observations the animals had been killed and serial sections of the hypothalamus, 25  $\mu$  thick, were made and stained according to the method of Klüver and Barrera (2). Positions of estradiol implantations were located on the basis of stereotaxic atlas of sheep hypothalamus (6).

#### RESULTS

The response to the estradiol implantations of castrated control ewes and castrated progesterone treated ones is presented in Fig. 1. The results obtained indicate that the castrated non treated ewes exhibit

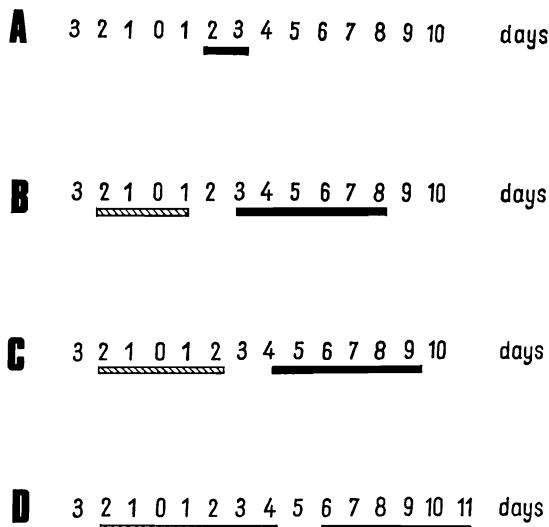


Fig. 1. Diagram showing the relationship between the effect of progesterone pretreatment and  $17\beta$ -estradiol implantation into the center of sexual behavior in the ewes. A, three castrated without progesterone treated ewes; B, C and D, three castrated with progesterone treated ewes. 0 denotes the days of implantations; horizontal hatched bars designate the days of progesterone injections; horizontal full bars, the days of behavioral estrus.

behavioral estrus on the second day following the estradiol implantation. The length of this behavioral estrus was 24-30 hr and its symptoms were rather weakly expressed; the ewes stood for service but did not show any manifestations such as interest in the ram or willingness to be teased as in the case of cyclic ewes during their physiological estrus. On the contrary, the ewes treated with progesterone did not exhibit any behavioral estrus after implantation of estradiol throughout the whole period of the treatment; although they showed strongly expressed symptoms of behavioral estrus on the 2nd day after the progesterone injections were stopped. The behavioral lasted for 3-6 days and the ewes themselves approached the ram and showed some manifestations such as sexual interest.

#### DISCUSSION

The investigations on disappearance rate of progesterone from the blood carried out with  $^{14}\text{C}$  or  $^3\text{H}$  labelled progesterone showed that practically all progesterone and its metabolite  $20\alpha$ -dihydroprogesterone disappear from the peripheral blood circulation during 3 hr following the i.v. injection of this hormone (4). On the basis of this statement it may be concluded that progesterone and its metabolite ( $20\alpha$ -dihydroprogesterone) disappeared completely from the circulating blood within 1st day after the progesterone treatment had been stopped. If so, the results of the described experiments on the castrated ewes, indicate that progesterone circulating in the organism suppresses the action of the implanted estra-

diol on the hypothalamic sexual behavior center. On the other hand the effect of the implanted estradiol on this center is significantly augmented on the day after progesterone disappearance from the blood circulation. This last phenomenon has been described in sheep even when estradiol was given peripherally after pretreatment with progesterone (3).

Since the estradiol implanted into the hypothalamic sexual behavior center had been acting locally, the described reaction of ewes might be thought as the effect of interaction of progesterone and estradiol displayed on the level of specific neuronal receptors of this center.

Thus, the experiments carried out on the castrated progesterone treated animals supported the suggestion that the lack of estrous behavior in the cyclic ewes following estradiol implantation into the hypothalamic sexual center, in the middle of estrous cycle, was caused by the suppressing action of progesterone on this center.

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