The Estrogen-sensitivity of the Vaginal Epithelia in Hypothyrosis

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During our earlier investigations we have observed changes in the estrogen metabolism as a result of hypothyrosis. The genital cycles are lengthened and the sensitivity of the organism towards exogenous estrogens is reduced. We performed experiments to determine whether a reduction of sensitivity to follicle hormone in the target organ, that is, in the vaginal epithelia, is produced by thyroidectomy.

For experimental purposes we have used partly animals with intact endocrine system and partly those which had been thyroidectomized and ovariec- tomized at the same time. We have performed hormonal treatments intravaginally with 4 I.U. of estrone. This dosage given intramuscularly did not produce estrus in hypothyrotic animals. On the other hand, when administered locally, it effected the cornification of the vaginal epithelia. The raising of the dosage lengthened the duration of the reaction.

Our experiments show that estrogen administered locally produces estrus in hypothyrotic animals. This reaction is effected even with the dosages which are ineffective intramuscularly. By raising the doses the time necessary to produce estrus diminishes, whereas its duration is lengthened. This phenomenon is common in the hypothyrotic as well as in the control animals. The changes of estrogen metabolism in hypothyrosis do not affect the sensitivity of the vaginal epithelia to estrogen.

Interhormonal correlations of the thyroid glands and ovaries were studied in our previous work, and it was found that hypothyrosis alters the estrogen metabolism. Following the thyroidectomy the genital cycles are lengthened and the estrogen-sensitivity of the organism decreases. The interhormonal regulation is connected with the functioning of the liver. The hypothyrotic animals do not react to small and medium dosages of estrogens; even large dosages cause only transitory effects. The problem arises as to whether the changed estrogen-sensitivity in hypothyrosis is due to a modified sensitiveness of the target organ, the vaginal epithelia. Berger, Lyons and Templeton, and Espinasse, reported that small doses of estrogens which do not cause any reaction
when given subcutaneously, produce the characteristic estrogen effect the cornification of the vaginal epithelia when applied locally in the wall of the vagina. According to Emmens, the amount of estriol required to produce estrus when given intravaginally is only 1/2,000th of that when given subcutaneously. According to Gardner, intravaginal injection method is suitable for detecting the threshold activity of estrogen.

Previously we have ascertained that when 4 I.U. of estrone acetate was applied intramuscularly it did not induce onset of estrus at all in hypothyrotic rats, whereas normal control animals showed estrus of 26 hours in duration. In the present experiments we have used the intravaginal injection method.

METHODS

Our experiments were performed in 4 groups of rats

Group A: On 30 rats we performed at the same time thyroidectomy and ovariectomy. After six weeks the animals received intravaginally a treatment with estrone acetate in 4 I.U./100 g bodyweight.

Group B: On 30 rats we performed at the same time thyroidectomy and ovariectomy. After six weeks the animals received a treatment with pure oleum helianthi. The aim of this experiment was to know whether intravaginal treatment has an effect on the cornification of vaginal epithelia. At the same time we examined whether the oil used for the dilution of estrone has no estrogenic effect.

Group C: This consists of 10 normal control animals which received 4 I.U./100 g estrone acetate intravaginally.

Group D: This consists of 10 normal control animals which received pure oleum helianthi intravaginally. The volume of injection was the same in each experiment.

The experiments were repeated with 8 I.U./100g estrone acetate. The aim of this was to find out whether by raising the hormone dose the duration and the latency before the appearance of the reaction are influenced.

In the other series of experiments we administered 25 I.U./100 g estrone acetate. This dosage produces estrus reaction, even when given intramuscularly, in 100% of the hypothyrotic animals.

RESULTS

The results of the intravaginal treatment with three different estrone dosages — comparing with the appropriate controls — are presented in Tables I and II. In hypothyrotic animals the estrus appeared 24 hours, on an average, later than in the controls when treated with 4 I.U. estrone. The duration of the reaction was only 8.3 hours, on an average, shorter in thyroidecomized animals. With 8 I.U. estrone, the reaction appeared earlier than with 4 I.U. in the hypothyrotic animals. The duration of estrus became longer in the both
groups, but in the thyroidectomized animals the duration was 11.2 hours, on an average, shorter than that in the control animals. When the dosage of estrone was increased to 25 I.U., the latent period was further shortened and the duration was further prolonged in the thyroidectomized group. However, there was a difference of 11.2 hours, on an average, in the duration of reaction between the thyroidectomized and control groups.

These results together with those obtained by intramuscular administration of the same dosages were summarized in Table II.
The oil used for dilution was ineffective by itself; the animals treated with oil showed no estrus.

DISCUSSION

In the present experiments we have confirmed that the estrogen-sensitivity of the vaginal epithelia can be studied better in castrated animals. The sensitivity of the peripheral target organs to the follicle hormone is altered by functional changes of the ovaries. The periodical changes of the genital cycle are eliminated by ovariectomy. Since the discoveries of Allen and Doisy, spayed animals are used for biological examinations and assays. Our experiments also proved that the castrated hypothyrotic animals were the most suitable.

In our previous work regarding the estrogen metabolism in hypothyrosis the question arose whether the reduced estrogen-affinity implies a reduced hormone-sensitivity of the target organ. Our experiments show that estrogen locally administered produces estrus in hypothyrotic animals. This reaction is effected even with the dosages which are intramuscularly ineffective. By raising the doses the time required to produce estrus diminishes, and the duration of reaction is lengthened. This phenomenon is common in the hypothyrotic as well as in the control animals.

From the data obtained by these experiments it is certain that the estrogen-sensitivity of the vagina is not strikingly reduced in hypothyrosis and estrogen dosage which was ineffective by intramuscular administration produces estrus when given intravaginally. The administration of higher dosages proportionally reduces the latent period before appearance of estrus. Thyroidectomized animals are thus capable of exhibiting appropriate reaction to follicle hormone administered locally. The changes in estrogen metabolism in hypothyrosis do not considerably affect the estrogen-sensitivity of the peripheral target organ.

References

4) Emmens, C.W. J. Endocr., 1941, 2, 444.