

THE EFFECT OF VARIOUS DOSES OF OESTRADIOL 17- β ON GLYCOGEN DEPOSITION IN THE RAT UTERUS, CERVIX AND VAGINA

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Summary. Administration of oestradiol benzoate, 5 to 200 μ g, intramuscularly daily for 3 days, results in glycogen deposition in the uterus and cervix of castrated Wistar rats. The relation between dose of oestrogen and amount of glycogen deposited is not, however, linear nor did all portions of the tract respond in a similar manner. The glycogen level of the vagina was not affected by the hormone administration, while progesterone lowered the glycogen content of all portions of the tract.

The glycogen metabolism of the mammalian female genital tract is briefly reviewed and discussed.

INTRODUCTION

Glycogen synthesis and deposition in the rat uterus with administration of various doses of oestradiol have been demonstrated (Bo & Atkinson, 1952; Rosenbaum & Goolsby, 1957; Boettiger, 1946). The glycogen is localized in the myometrium and only with doses of 10 μ g was it possible to demonstrate it histochemically in the endometrium. The enzyme kinetics of glycogen synthesis in the rat uterus is a first order reaction rate (Bitman, Cecil, Mench & Wrenn, 1965) with maximal synthesis occurring with 1 μ g of subcutaneously administered oestradiol.

In the mouse female genital tract, glycogen content differs both during the oestrous cycle and within portions of the tract. Uterine glycogen levels are maximal at pro-oestrus and oestrus while vaginal glycogen is maximal at metoestrus and minimal at oestrus (Balmain, Biggers & Claringbold, 1956).

In the investigations of oestrogen-induced genital tract glycogen synthesis performed so far, one or two levels of oestrogen have been used and the investigation has been restricted to a single portion of the tract. The possible interrelationships of genital tract glycogen deposition with increasing doses of oestradiol and in all portions of the tract has not been evaluated.

MATERIALS AND METHODS

A total of 110 female Wistar rats, weighing 150 to 200 g, were used. The animals were spayed and rested for at least 7 days before being randomly assigned

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to an experimental group. The animals in each experimental group received either 0, 5, 25, 50, 100 and 200 μg of oestradiol benzoate or 1 mg of progesterone intramuscularly for 3 days. On the 4th day, the animals were killed, the genital tract rapidly removed, separated, weighed, placed in a solution of 30% KOH and digested for 20 min. Glycogen was determined by the anthrone method (Seifter, Dayton, Novic & Muntwyler, 1950) and results expressed as μg of glycogen/100 mg wet weight of tissue.

RESULTS

The glycogen levels of the genital tract are listed in Table 1. In the spayed animal, the uterine and vaginal glycogen levels were of similar magnitude, while cervical tissue contained about one-half of the amount.

A standard analysis of variance demonstrated significant differences in

TABLE 1
AVERAGE μg OF GLYCOGEN/100 mg AND S.E. OF (WET WEIGHT) TISSUE FROM THE FEMALE RAT GENITAL TRACT OF SPAYED RATS RECEIVING INCREASING DOSES OF OESTROGEN OR 1.0 mg OF PROGESTERONE

	Treatment						
	Oestrogen (μg of oestradiol benzoate)						Progesterone
	0	5	25	50	100	200	
No. of animals	10	10	20	20	20	20	10
Uterus	56.3 \pm 10	57.8 \pm 5	154.8 \pm 15	146.3 \pm 13	123.6 \pm 11	129.7 \pm 10	35.8 \pm 5
Cervix	30.8 \pm 3	67.7 \pm 12	96.0 \pm 15	61.0 \pm 6	65.4 \pm 9	75.4 \pm 12	21.5 \pm 4
Vagina	61.0 \pm 9	50.3 \pm 7	58.6 \pm 5	56.9 \pm 7	43.4 \pm 5	44.2 \pm 8	40.8 \pm 5

amounts of uterine glycogen with all doses of oestradiol greater than 5 μg . No statistical differences between the spayed and 5 μg level were observed when Duncan's Multiple Range Test (Harter, 1960) was applied to make all possible comparisons with all oestrogen levels. Oestradiol dosages above 5 μg increased the levels of uterine glycogen significantly ($P < 0.01$), but not in a linear fashion. The average glycogen levels of the oestrogen groups above the 25 μg dose were lower, but not significantly so.

The cervical glycogen was significantly increased above the spayed level ($P < 0.05$) with administration of oestradiol. Maximum deposition was observed with 25 μg dose and no further increases with higher doses of oestradiol occurred. No significant changes in vaginal tissue glycogen were demonstrated in oestrogen-administered animals, as compared with controls.

The administration of 1 mg of progesterone had a glycogenolytic effect and decreased the glycogen content to below spayed levels in all portions of the tract, though in no case was the difference significant ($P = 0.1$).

DISCUSSION

The results demonstrate that the female rat genital tract tissue does not respond to increasing levels of oestrogen with subsequent increases in glycogen deposition in all tissues. Uterine glycogen synthesis is maximal at the 25 μg dose and increasing oestrogen levels did not result in increased glycogen deposition. Other workers have demonstrated maximal deposition 24 hr after administration of a single dose of 1 μg of subcutaneously administered oestradiol with subsequent decreases in synthesis 48 hr later (Bitman *et al.*, 1965). These differences in amounts of oestrogen for maximum synthesis may be due to the methods used, i.e. 3 days' oestrogen therapy rather than a single dose, and intramuscular as opposed to subcutaneous administration.

The cervical tissue reaction was intermediate between those of the uterus and vagina. With the exception of the spayed and 5 μg levels, the glycogen levels were all greater than vaginal levels, but less than uterine. A similar reaction has been observed with the epithelial structure of the rat cervix during various phases of the oestrous cycle (Hamilton, 1947).

The synthesis of mammalian genital tract glycogen either during the reproductive cycle or with administered hormones exhibits great species differences. In the primate, whose reproductive cycles are of relatively long duration, the uterine glycogen is maximal at the secretory phase (VanDyke & Ch'en, 1936; Zondek & Stein, 1940) but, in the rodent, with short, frequent cycles, the uterine glycogen synthesis is dependent on oestradiol (Bo & Atkinson, 1952; Rosenbaum & Goolsby, 1957).

Information on cervical glycogen content in the experimental animal is lacking. In the human, cervical glycogen has been described as either minimal or absent (Simon, 1934; Atkinson, Shettles & Engle, 1948) and cervical mucus glycogen is lowest at the time of ovulation (Pommerenke, 1946; Breckenridge & Pommerenke, 1951).

The primate vaginal glycogen varies with the cycle (Corner, 1923) and anatomical location (Rakoff, Feo & Goldstein, 1944). Early workers, using histochemical methods, could not demonstrate glycogen in the vaginal tissue of the pig, lamb, squirrel (Bremicker, 1927), cat, rat, dog, rabbit, guinea-pig or cow (Cruickshank & Sharman, 1934). Mouse vaginal glycogen deposition, however, is cyclic, not maximal at the period of mitotic activity but at the period of cornification. The greatest amounts are in the region immediately under keratin formation—the stratum spinosum (Balmain *et al.*, 1956) suggesting a possible role in keratin formation.

The polymers of glucose, maltotetraose, maltotriose, maltose, as well as glucose, products of enzymatic breakdown of glycogen (Torres & Olavarria, 1961), have been isolated in human vaginal fluid and epithelium (Sumawong, Gregoire, Johnson & Rakoff, 1962; Gregoire, 1963). These oligosaccharides are also present in the entire rabbit genital tract (Gregoire & Gibbon, 1965) where they were increased with oestrogen and decreased with progesterone administration. The presence of these compounds suggests that glycogen may be hydrolysed to simpler products and utilized as energy source for activity of the reproductive tract or utilization by the gametes.

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