THE CONTRACEPTIVE ACTION OF IMPEDING OESTROGENS

VII. EFFECTIVENESS OF OESTRIOL IN THE RABBIT AND THE HAMSTER

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It has previously been shown that oestriol can exert a complete contraceptive effect when given both before and after coitus in the rat, and can also act by way of semen transference. Because of the low concentration of oestriol (0.0125 mg/day) required, the fact that this steroid worked when administered *post coitum*, and the findings of previous studies (Brecher & Wotiz, 1967, 1968; Scublinsky & Wotiz, 1971; Wotiz, Smith, Shapiro & Scublinsky, 1971), it was proposed that the contraceptive action was due to alteration of the endometrial milieu resulting in prevention of implantation in this species.

This paper presents the findings of an investigation carried out to see whether contraception can be achieved in animals which do not have oestrous cycles, or oestradiol surges, resembling those which occur in the rat. Rabbits, which are neuro-ovulators, and hamsters, which do not have an oestrogen surge at the time of implantation (Prasad & Kalre, 1967), were selected. These species are particularly interesting since, in both, implantation may be induced without oestrogens and, in the hamster, various antioestrogens do not prevent implantation (Prasad & Kalre, 1967).

Eight, female, 8- to 9-week-old golden hamsters were mated on the day of pro-oestrus by exposure to eight male animals. Mating was verified by visual observation, and its success determined by detection of spermatozoa in the vaginal smear. On the following morning, subcutaneous injections of 0.05 mg of oestriol dissolved in 0.2 ml of sesame oil (four experimental animals) and 0.2 ml of sesame oil (four control animals) were given. Injections were continued daily for a total of 4 days. On the 10th day after mating, the animals were killed, the uteri removed, and the number of implantation sites recorded. The control group showed an average implantation density of 6.75 implants/horn. The average number of implantation sites (6.0) did not vary significantly in the experimental animals.

A second experiment involving twelve animals was carried out exactly as above, except that the dosage of oestriol injected was increased to 0.1 mg/day in one group of four animals and to 1.0 mg/day in another group. The injections were continued for a total of 7 days following mating. The results are shown in Table 1.

Eight female rabbits, weighing approximately 5 kg each, were mated to one buck. Mating was verified by visual observation and detection of ejaculate at the vulva. Following mating, four of the animals received daily subcutaneous injections of 0.5 ml of sesame oil for 7 consecutive days and four others were treated similarly, except that the oil contained 1 mg of oestriol. On the 11th day after mating, the animals were killed, the uteri removed to observe the number of implantation sites and the ovaries were examined under a dissecting microscope for corpora lutea. The data are summarized in Table 2.

TABLE 1
OESTRIOL AND INHIBITION OF IMPLANTATION IN THE HAMSTER

<i>No. animals</i>	<i>Treatment</i>	<i>Pregnancies</i>	<i>Average no. implantations</i>
4	None	3	6.7
4	0.1 mg oestriol	0	0
4	1 mg oestriol	0	0

TABLE 2
OESTRIOL AND INHIBITION OF IMPLANTATION IN THE RABBIT

<i>Animals</i>	<i>Treatment</i>	<i>Pregnancies</i>	<i>Average no. implantations</i>	<i>Average no. corpora lutea</i>
4	None	4	6.5	7
4	1 mg oestriol/day	0	0	5

The most important single aspect of the work described here is the fact that relatively low doses of oestriol appeared to be as fully effective an anti-implantational compound in the rabbit and the hamster as in the rat. It is difficult to judge what specific effect is responsible for this action in these two species. While a good case for the antioestrogenic effect of oestriol could be made in the rat (Huggins & Jensen, 1955; Wicks & Segal, 1956; Hisaw, 1959; Emmens & Finn, 1962), the same arguments do not necessarily apply here. Neither the hamster nor the rabbit appears to require oestrogenic preparation of the endometrium since removal of the ovaries still allows implantation in the absence of supportive oestrogen therapy (Prasad & Kalre, 1967). On the other hand, this does not necessarily preclude the rôle of oestriol as an antioestrogen since extragonadal sources may contribute to the total oestrogen pool in these animals and adrenal compensatory mechanisms might be operational. The presence of an oestradiol-specific receptor which has been demonstrated in the rabbit uterus (Korenman, 1969), and which is analogous to that in the rat, suggests a similar rôle for oestrogens in this animal.

That oestriol, as an antioestrogen, acts differently from the pharmaceutical antioestrogens is suggested by the fact that the former is effective as an anti-implantation agent in the hamster while the latter are not. In general, these neutral steroidal antioestrogens do not bind to, or compete with oestradiol for the specific receptors.

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