

# EFFECT OF OVARECTOMY, INJECTION OF ESTROGENS, AND ORAL ADMINISTRATION OF CHOLESTEROL ON THYROID FUNCTION AND EKG OF RABBITS

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Experiments were carried out on 32 normal and 31 ovariectomized rabbits, aged one month. An increase in the serum cholesterol concentration was found in the rabbits after ovariectomy and also after oral administration of cholesterol to ovariectomized and intact animals. This increase persisted for 3 months of the experiment and was accompanied by a decrease in absorption of  $I^{131}$  by the thyroid of these animals. Injection of estradiol dipropionate into ovariectomized and intact rabbits receiving cholesterol led to a decrease in the blood cholesterol level. The most marked changes in the EKG were detected in ovariectomized rabbits receiving oral cholesterol.

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Changes in the EKG in the level of thyroid function, and in the degree of development of hypercholesteremia and atherosclerosis of the aorta were studied in rabbits after ovariectomy, oral administration of cholesterol, and injection of estradiol dipropionate into the animals [1-26].

## EXPERIMENTAL METHOD

Experiments were carried out on 63 sexually immature female rabbits. Ovariectomy was performed on 31 animals at the age of one month (weight 700-900 g). Three months after the operation, the ovariectomized and normal intact animals of the same age were divided into four groups: 1) control, 2) receiving estradiol dipropionate in a dose of 0.02 mg/kg intramuscularly, three times a week for three weeks; 3) receiving cholesterol by mouth in a dose of 0.12 mg/kg daily for three months; 4) receiving cholesterol and estradiol dipropionate simultaneously in the same doses as those in groups 2 and 3. The EKG was recorded by needle electrodes in standard and amplified monopolar leads from the limbs with the rabbits in the prone position. The serum cholesterol concentration was determined in all rabbits monthly and the absorption of  $I^{131}$  by the thyroid was determined. This latter procedure was done 2, 5, 24, and 48 h after intramuscular injection of the isotope in a dose of 0.5  $\mu$ Ci. The percentage of absorption of  $I^{131}$  by the thyroid was estimated against a standard taken as 100%.

The rabbits were sacrificed 6 months after ovariectomy, the aorta was stained in toto with Scharlach red and studied macroscopically, and the uterus was weighed.

## EXPERIMENTAL RESULTS

The dose of estradiol dipropionate used was evidently close to physiological, because the weight of the uterus in the ovariectomized rabbits receiving estradiol dipropionate was equal to the weight of the uterus in normal animals of the same age.

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Comparison of changes in the lipid indices with those in thyroid function showed that two months after ovariectomy the serum cholesterol concentration was raised (from  $59 \pm 2$  to  $119 \pm 8.8$  mg%) and there was a corresponding decrease in the maximal absorption of  $I^{131}$  by the thyroid (from  $26.80 \pm 4.44$  to  $15.31 \pm 0.83\%$ ;  $P < 0.001$ ) determined in 31 ovariectomized rabbits two months after the operation.

The blood cholesterol level 6 months after ovariectomy was no higher in the ovariectomized rabbits than in normal animals of the same age. The character of  $I^{131}$  absorption by the thyroid at this period was similar to that in the controls, but the absolute value of its maximal absorption remained significantly ( $P < 0.05$ ) below its maximal value in the control rabbits of the same age (24 h after iodine administration  $19 \pm 2.13\%$  in the ovariectomized and  $26.8 \pm 4.44\%$  in the control animals). Absorption of  $I^{131}$  by the thyroid in both the intact and the ovariectomized rabbits receiving cholesterol by mouth was reduced ( $320 \pm 38$  mg%), but the difference compared with the control ( $479 \pm 2.3$  mg%) was not statistically significant.

Injection of estradiol dipropionate into the ovariectomized rabbits raised their blood cholesterol concentration slightly by comparison with the control. Absorption of  $I^{131}$  by the thyroid during the first few hours and days after its injection remained lower than in the control animals. The maximal value of iodine absorption in these rabbits occurred at 48 h, and not at 24 h as in the control, but in its value it was closer to the control figure. In intact rabbits, injection of estradiol caused no significant changes either in the serum lipid indices or in the thyroid function.

Thyroid function likewise was not significantly changed in the rabbits receiving cholesterol and estradiol dipropionate, although in these animals there was a marked increase in the blood cholesterol level.

The protein-bound iodine was determined before the experiment and before sacrifice in 10 intact rabbits receiving cholesterol. No significant differences were found in this index (mean value before cholesterol administration  $2.3 \pm 0.09$ ; at end of experiment  $2.1 \pm 0.1$ ).

Despite the high blood cholesterol level ( $479 \pm 2.3$  mg%), deposition of lipids in the wall of the aorta in ovariectomized rabbits receiving oral cholesterol was moderate, just as in the case of animals of other groups receiving cholesterol by mouth [8]. The resistance of the aortic wall to deposition of lipids in the animals investigated was evidently due to the fact that they were young (7 months of age).

The EKG of the young rabbits before the experiment began was practically indistinguishable from the EKG of healthy rabbits [9, 10]. Predominance of the vertical and right types of disposition of the electrical axis of the heart was noted.

In the group of ovariectomized rabbits receiving cholesterol, a gradual increase in size of the T wave was observed 4 and 6 months after the beginning of the experiment, and in individual animals, in the standard leads, it was considerably higher in voltage than in the largest R wave, and sometimes became bimodal; a negative or biphasic T wave appeared in the AVF leads. In some animals a sharp increase in size of the R wave was found in all leads, with the appearance of a large Q wave in leads I, II, and AVF. One rabbit developed permanent ventricular extrasystoles 6 months later.

In the intact rabbits receiving cholesterol, changes in the EKG developed much later and were less well defined. In the animals of the other groups, no changes in the character of the EKG could be observed. The absence of marked changes in EKG in the ovariectomized rabbits receiving cholesterol and estradiol dipropionate, compared with the group of animals not receiving estradiol after ovariectomy, could evidently be attributed to the protective effect of estradiol, inhibiting the development of atherosclerosis [7, 8].

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