THE RELATION OF BLOOD CHOLESTEROL AND THE SIZE OF PROSTATIC AND VESICULAR TRANSPLANTS IN THE ANTERIOR CHAMBER OF THE EYE

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The relationship of certain endocrine glands to the blood cholesterol is well established. Denis (1) found that in Graves' disease there was hypocholesterolemia and the reverse in myxedema. Westra and Kunde (2) secured similar results in experimental animals, when the higher values in cretin rabbits were lowered by the feeding of desiccated thyroid.

It has been clearly established by the studies of Slemons and Stander (3), Boyd (4) and others, that there is an increase in the free and total plasma cholesterol in pregnancy. Okey and Boyden (5) reported that the blood cholesterol was conspicuously and consistently lowered during or within a few days before menstruation. The attempt has been made, with doubtful success, to relate these changes in blood cholesterol to the available active estrin in the body.

In view of the conspicuous increase in the size of prostatic and vesicular transplants following injections of estrin in the male rabbit reported in the preceding papers (6, 7), it seemed desirable to investigate the level of the blood cholesterol during the period of the enlargement. Since other hormones also caused enlargement, it was of interest to study these two factors under the influence of the male sex hormone and the anterior pituitary-like substance of pregnancy urine.

Methods

The procedures described in the preceding papers (6, 7) were used for the transplantation and measurement of the grafts in the eyes of male rabbits. Free cholesterol was determined according to the blood lipid methods of Kirk, Page and Van Slyke (8). Briefly, the method consisted in the carbon combustion of the material precipitated by digitonin from the alcohol-ether and petroleum ether soluble extractives of heparinized plasma. The carbon dioxide liberated by wet combustion was collected and determined by manometric methods.
The rabbits were fed a diet of hay, oats and water, and a constant quantity of lettuce was given each day. No food was given for at least 16 hours before the blood samples were taken. Blood was collected from the ear vein into calibrated tubes in order to keep the dilution by the heparin constant. The plasma was removed after centrifugation and extracted with alcohol and ether.

**Text-FIG. 1.** Transplant size and blood cholesterol with the injection of the female sex hormone.

The effect of this daily loss of blood was studied in order to eliminate it as a significant factor in any changes observed. After from 2 to 3 weeks of the experimental procedure, there was an average fall of 20 per cent in the hemoglobin value (Dare) but no change in the serum proteins. In animals in which no hormone injections were given, there was no consistent trend in the lipid values and it is improbable that this anemia was of importance in the results.
Preliminary experiments, in which total lipid carbon was determined, showed no significant correlation between this value and the size of the transplants.

RESULTS

The Female Sex Hormone.—In Text-figs. 1 and 2 are shown a typical response of a vesicular transplant and the blood cholesterol to an injection of the female sex hormone. The results in Text-fig. 2 are arranged so that the determinations of size, shown in Text-fig. 1, are advanced 1 day. There was a prompt increase of the blood cholesterol.
level which was followed in 24 to 48 hours by an increase in size of the transplant, as described in the preceding paper. When the values for each day were analyzed (Text-fig. 1), the correlation coefficient was +0.091 with a probable error of 0.37. In sharp contrast was the correlation coefficient of +0.512 with a probable error of 2.25, when the size was advanced 24 hours (Text-fig. 2). It should be noted that the secondary rise in size during the recovery period was also correlated with an increase of the blood cholesterol. This elevation of cholesterol was also found in the castrated animal when the female sex hormone was injected, although in general it was not as conspicuous.
The Gonadotropic Substance of Pregnancy Urine.—In Text-fig. 3 are the results in an intact animal, which had not received a previous injection. The transplant undergoes the usual response, which has been described, but there was no alteration in the cholesterol values. In the castrated animal neither the transplant size, nor the cholesterol, was significantly affected.

Male Sex Hormone.—In the intact animal (Text-fig. 4), there was a slight increase in the size but no effect on the cholesterol in response to the male sex hormone. In the castrated animal, a moderate effect on the transplant was observed, but no change in the cholesterol values.

Ingestion of Cholesterol.—Two animals were given by stomach tube 0.5 gm. of pure cholesterol dissolved in sunflower oil, on 3 consecutive days. In both, there was an increase in the blood cholesterol comparable to that which results from administration of the female sex hormone, but no significant alteration in the size of the transplant.

Discussion

It is clear that of the three hormones, the male and female sex hormones and the extract of pregnancy urine, which cause significant
changes in the size of vesicular and prostatic transplants in the eye, only one, the female sex hormone, provokes a correlated increase of blood cholesterol. It is also clear that the presence or absence of the testes is of no significance in this correlation.

There are two possible conclusions: first, that the female sex hormone acts on two mechanisms to produce, on the one hand, changes in the prostate, and, on the other hand, alterations in the metabolism of cholesterol; and second, that a single effect in the rabbit is manifested in two different ways. The fact that other hormones produce indistinguishable increases in the size of the transplant but no elevation of cholesterol, indicates that the former conclusion is correct. This is further supported by the observation that increase of blood cholesterol by feeding does not carry with it changes in the transplants.

SUMMARY

In male rabbits, injections of the female sex hormone result in marked increase in the size of ocular transplants of the prostate and seminal vesicles and a correlated elevation of the blood cholesterol.

Other hormones, which cause an increase in the size of the transplants, do not show this correlation.

The ingestion of cholesterol with conspicuous increase of the blood cholesterol, has no effect on the size of the transplants.

BIBLIOGRAPHY

1. Denis, W., J. Biol. Chem., 1917, 29, 93.