ARTERIOVENOUS GLUCOSE DIFFERENCE MEASUREMENTS ON THE RABBIT OVARY

By

Erik Odeblad and Göran Enhörning

The biochemical processes connected with steroid hormone formation in the ovary are of great interest. If these processes are associated with energy requirement, it is possible that glucose—directly or indirectly—forms a source of energy. Consequently it seems interesting to investigate, whether there is any arteriovenous glucose difference in the ovary during various functional phases.

Arteriovenous difference measurements of glucose have been performed previously o. a. on upper extremity but have not been performed on the ovary. In a preliminary report (Enhörning, Fagerholm & Odeblad, 1950), no clear glucose differences between ovarian artery and vein was found; in this paper the question is subjected to a more careful investigation.

EXPERIMENTAL

From each of 12 rabbits a total of 166 arterial and ovarian venous specimens were taken, making it possible to calculate 73 difference values.

The rabbits were divided into three groups, and given the following hormonal treatment. Group I consisted of 4 rabbits, each of which received 300 I. U. human chorionic gonadotrophin (Pregnyl, Pharmacia) 10 days before use. The ovaries thus were in a »secretory inactive state«, pale in colour and containing large amounts of cholesterol. The uterus was pale, thin and relaxed. In Group II rabbits were treated in the same way and received, in addition, 400 I. U. pregnant mare serum gonadotrophin (Gestyl, Pharmacia) about 1 hour before the first specimen was taken. The ovary was thus brought into an oestrogen secretion phase and was hyperaemic. The uterus was still pale, thin and relaxed. In Group III 4 rabbits treated as in group I were given the...
The same dose (400 I. U.) pregnant mare serum gonadotrophin 24 hours before use. The ovary had now passed through the state of active oestrogen secretion, and was considered to be exhausted. The uterus was red and engorged and showed increased motility and excitability. The ovaries of all animals weighed 600–800 mg. and contained 5–10 young corpora lutea.

When taking the specimens the animals were anesthetized with 2 per cent sodium isopropyl bromallyl-N-methylmalonylcarbamide (Narkotal, Astra) and 16 per cent urethane. By lateral laparotomy the ovarian vein was exposed for puncture. Anastomoses to adjacent organs were ligated. The venous blood was collected quantitatively by puncture. The volume of the specimen and the time required to take it were measured. Arterial specimens were taken from mesenteric arteries. The technique has previously been described in detail (Odeblad, 1951).

When all specimens were taken, the ovaries were examined histologically with haemalum-eosin staining and in polarized light. In group I the interstitial gland contained large amounts of birefringent granules, in group II the amount seemed somewhat less, judged by subjective estimation. In group II no birefringent granules were found in the interstitial gland. No other histological differences were found in the ovaries.

In the blood samples, showing no signs of hemolysis, glucose was determined according to Folin & Svedberg (1930) with photoelectric colorimetry using a Hilger spectrophotometer and filter 606 after calibration. Twenty measurements on a single specimen showed an error of method of 0.043 mg./ml., at a mean value of 1.245 mg./ml. (3.5 per cent). In this investigation the rate of glucose exchange in the ovary expressed in mg./min. has been determined. The standard deviation of one exchange rate measurement, calculated on the whole material, was 0.115 mg./min., which corresponds to 0.115 mg./ml. at a velocity of 1 ml./min.

**THEORETICAL**

The exchange rate has been determined according to the Fick principle. During the time interval $dt$ (time in minutes) the exchange of a substance, $dU$, in mg. of an organ is

$$dU = W(C_a - C_v) dt. \quad (1)$$

where $W$ is the velocity of circulation in ml./min. and $C_a$ is the arterial concentration and $C_v$ the venous concentration in mg./ml. By integration we receive the exchange $U_I$ during the time interval $(t_2 - t_1)$:

$$U_I = \int_{t_1}^{t_2} WC_a dt - \int_{t_1}^{t_1} WC_v dt \quad (2)$$

$$(t)$$

75
In the time interval \( t_2 - t_1 = t_f \), the exchange per unit time \( E \) (exchange rate) is, accordingly:

\[
E = \frac{U_f}{t_f} = \frac{\alpha}{t_f} - \frac{\omega}{t_f} = A - V \tag{3}
\]

The definition and calculation of \( A \) and \( V \) are given below.

The present investigation has been so arranged that the integral \( \omega \) has been exactly determined, and the integral \( \alpha \) has been approximately determined. This seemed justifiable since the integral \( \omega \) was expected to be more than \( \alpha \) and because a longer time was required to obtain a satisfactory amount of venous blood than of arterial blood.

The integral \( \omega \) is apparently the amount of glucose, present in the syringe after the puncture was finished. We can therefore introduce

\[
V = \frac{\omega}{t_f} = W_v \cdot C_v \tag{4}
\]

where \( W_v \) is the mean velocity during the time interval \( t_f \) and \( C_v \) is the mean venous glucose concentration in the syringe.

In the same way, we can write

\[
A = \frac{\alpha}{t_f} = W_a \cdot C_a \tag{5}
\]

Here \( W_a \) is apparently equal to \( W_v \), (because blood would otherwise accumulate in the organ, or it would be emptied of blood). \( C_a \) has been calculated by interpolation between two adjacent arterial determinations.

We can therefore finally write

\[
E = A - V = W_v \cdot (C_a - C_v) \tag{6}
\]

By determination of repeated arterial and venous glucose concentrations, and measuring of the volumes of the venous specimens and the time required for taking these specimens, it was thus possible to calculate consecutive values of the exchange rate of glucose in mg./min. of a single ovary.

**RESULTS**

In all groups the mean venous levels have been lower than the mean arterial levels.

The exchange rate in group I («resting ovary») was found to be \( 0.15 \pm 0.12 \) (mean error) mg./min.
In group II («working ovary») the exchange rate was found to be 0.13 ± 0.09 mg./min.
In group III («exhausted ovary») the exchange was 0.09 ± 0.06 mg./min.
On the whole material the exchange rate was 0.123 ± 0.051 mg./min.
As a rule, the glucose concentrations in both arterial and venous blood rose somewhat during the operation.

DISCUSSION

As in most earlier measurements of arteriovenous glucose differences, this investigation has shown that such differences are very small, if present at all. The whole material probably supports the existence of a glucose consumption of 0.123 ± 0.051 mg./min. in the ovary. No differences between the functional groups were found.

The four most important structures in the ovary are: the supporting tissues, the interstitial gland, the follicles and the corpora lutea. Only the interstitial gland showed a histo-chemical difference between the three groups. The difference may be due to active processes in this part of the ovary. However, the corpora lutea have been shown to possess a considerable glycolytic activity (Copenhaver, Meyer & Mc Shan, 1949) and several corpora lutea were as a rule present in the ovaries. In this connection the finding that the glycogen content of the interstitial gland rapidly decreases in secretory activity is of great interest (Höffelt, 1951). Here too another question has to be considered in an already complex problem. It has repeatedly been pointed out that the ovarian hormones take part in some way in the regulation of sugar metabolism (Bianchi, 1950, Blöch & Bergel, 1933, 1935, Högler & Zell, 1949, Kocsár & Kesztyüs, 1951, Rowe, Mc Manns & Plummer. 1935). It is therefore not impossible that the occurrence of steroid hormones in the ovary in oestrogen secretory activity might cause local changes in the glucose exchange. However, the present investigation does not support the existence of such changes.

In the interpretation of the present results it must also be borne in mind that other substances possessing the capacity to reduce alkaline copper tartrate solution, such as glutathione, creatinine and uric acid, might be present to some unknown extent in arterial and venous blood.

The conclusion, that may be drawn from this investigation is that a small arteriovenous glucose difference probably exists in certain functional phases of the rabbit ovary.

SUMMARY

In 12 rabbits 73 ovarian arteriovenous difference values of glucose were determined according to Folin & Wu. Suitable experimental and theoretical methods
were developed to determine the exchange rate of glucose in mg./min. The phases of oestrogen secretory rest, oestrogen secretory activity and exhaustion were produced artificially and examined. No differences were found between these functional stages. In the whole material, the exchange rate was 0.123 ± 0.051 mg./min. It is possible that the differences may be due to substances other than glucose.

REFERENCES