Blood flow to the genital tract of oestrous and dioestrous guinea-pigs

P.-O. B. Sjöquist, L. Bjellin and A. M. Carter*

*Department of Zoophysiology, University of Lund, Helgonavägen 3B, S-223 62 Lund, Sweden, and *Department of Physiology, University of Odense, Niels Bohrs Allé, DK-5000 Odense, Denmark*

Summary. Ovarian, uterine and vaginal blood flow were determined in 22 virgin guinea-pigs by the tracer microsphere technique. Measurements were made during oestrus, when cornified cells appeared in the vaginal smear (Day 1), or during the luteal phase of the cycle (Day 11). The total rate of blood flow to the genital tract was $0.58 \text{ ml. min}^{-1}$ on Day 11 and $2.92 \text{ ml. min}^{-1}$ on Day 1. This difference was largely due to an 8-fold increase in uterine blood flow from 0.26 to $2.01 \text{ ml. min}^{-1}$. Although uterine weight increased over the same period, there was a significant increase in uterine tissue perfusion from 0.32 to $1.18 \text{ ml. min}^{-1} \cdot \text{g}^{-1}$. The vagina exhibited a similar pattern, including a significant increase in tissue perfusion. Ovarian blood flow decreased from a value of $0.19 \text{ ml. min}^{-1}$ during the luteal phase to $0.10 \text{ ml. min}^{-1}$ at oestrus. Perfusion of the ovarian tissue was considerably greater on Day 11 than on Day 1 (2.86 versus $1.39 \text{ ml. min}^{-1} \cdot \text{g}^{-1}$).

Introduction

The tracer microsphere technique for determination of organ blood flow readily lends itself to the study of circulation in small mammals. We have previously used this technique to measure regional blood flow in pregnant guinea-pigs (Bjellin, Sjöquist & Carter, 1975; Sjöquist, Bjellin & Carter, 1977) and have now applied the same method to determine ovarian, uterine and vaginal blood flow in oestrous and dioestrous animals.

Materials and Methods

The virgin guinea-pigs used in this study weighed between 450 and 675 g. Each had a regular oestrous cycle of 16–18 days as determined by daily observation for vaginal opening and the staining of vaginal smears. The day on which cornified epithelial cells appeared in the smear was designated Day 1 of the cycle. Ten animals were examined on Day 1; in most of these rupture of the vaginal membrane had been observed 24 h previously. Twelve animals were examined on Day 11 of the cycle.

General anaesthesia was induced by the intraperitoneal injection of sodium pentobarbitone (30 mg. kg^{-1} body weight) and artificial ventilation was supplied through a tracheal cannula, following the recommendations of Kleinman & Radford (1964). The left ventricle and both femoral arteries were catheterized as previously described (Sjöquist *et al.*, 1977). One of the femoral catheters was connected to a pressure transducer and electromanometer to enable registration of the arterial blood pressure.

Organ blood flows were determined by the reference sample method (Makowski, Meschia, Droegemueller & Battaglia, 1968). The microspheres used had a diameter of $15 \pm 5 \mu\text{m}$ and were labelled with ^{141}Ce (3M Co., St. Paul, Minnesota, U.S.A.). They were suspended in 10% dextran, to which a drop of Tween 80 was added to prevent their aggregation. Between 4×10^5 and 10×10^5 microspheres were injected into the left ventricle. The suspension was agitated by ultrasound immediately before the injection, which took 30–35 sec. Starting 10 sec before the microsphere infusion and ending 15 sec afterwards, a reference sample of blood was withdrawn at a constant rate ($0.84 \text{ ml. min}^{-1}$) from one of the femoral arteries. The animal was then killed and the ovaries,

uterus and vagina were dissected free of connective tissue and fat. The kidneys were also removed for subsequent comparison of left and right renal perfusion. The blood flow of each organ was calculated from its content of ^{141}Ce relative to that of the reference sample of blood as previously described (Bjellin *et al.*, 1975). The number of microspheres in each ovary varied between 500 and 1200 and there were many more in the samples of vaginal and uterine tissue.

In the text, mean values are stated together with their standard errors. The statistical significance of differences in blood flow was assessed by Student's *t* test.

Results

Guinea-pigs on Days 1 and 11 of the oestrous cycle had a similar blood pressure and heart rate. Mean arterial blood pressure for the entire group was 7.0 ± 0.1 kPa (53 ± 1 mmHg) whilst the heart rate was 4.2 ± 0.1 Hz. There was a satisfactory correlation between the perfusion rates of the left and right kidneys ($r = 0.93$), indicating an even distribution of the injected microspheres.

The total rate of blood flow to the genital tract is shown in Table 1, together with the distribution of blood to the uterus, vagina and ovaries. The flow rate was greater on Day 1 than on Day 11, largely due to an 8-fold increase in uterine blood flow. The augmentation of uterine blood flow reflected the enlargement of the uterus but there was also a significant increase in tissue perfusion. The vaginal blood flow patterns were similar to those of the uterus. Ovarian blood flow, however, was less on Day 1 than on Day 11. No corresponding difference in ovarian weight could be detected; perfusion of the ovary was thus greater on Day 11 than on Day 1.

Table 1. Weight (g), blood flow ($\text{ml} \cdot \text{min}^{-1}$) and tissue perfusion ($\text{ml} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$) of the ovaries, uterus and vagina of oestrous (Day 1) and dioestrous (Day 11) guinea-pigs

	Day 1 (N = 10)	Day 11 (N = 12)	Statistical significance
Ovaries Weight	0.07 ± 0.01	0.07 ± 0.01	N.S.
Blood flow	0.10 ± 0.02	0.19 ± 0.02	$P < 0.01$
Tissue perfusion	1.39 ± 0.08	2.86 ± 0.48	$P < 0.01$
Uterus Weight	1.67 ± 0.11	0.81 ± 0.04	$P < 0.001$
Blood flow	2.01 ± 0.30	0.26 ± 0.03	$P < 0.001$
Tissue perfusion	1.18 ± 0.10	0.32 ± 0.03	$P < 0.001$
Vagina Weight	0.81 ± 0.03	0.37 ± 0.02	$P < 0.001$
Blood flow	0.82 ± 0.16	0.12 ± 0.02	$P < 0.001$
Tissue perfusion	1.01 ± 0.19	0.31 ± 0.05	$P < 0.001$
Total blood flow	2.92 ± 0.43	0.58 ± 0.05	$P < 0.001$

Values are mean $\pm$ S.E.M.

Discussion

The uterine and ovarian arteries of the guinea-pig anastomose on each side to form a continuous arterial loop (Egund & Carter, 1974). Chaichareon, Rankin & Ginther (1976) indicate that the ovarian artery provides most of the blood supply to the cranial third of the uterus and about 40% of that to the middle third of the horn. We found a considerable difference between oestrous and dioestrous guinea-pigs in the rates of perfusion of the ovaries, uterus and vagina, involving a change in the total rate of blood flow through the four arteries and in its distribution. The endocrinological background to this variation is exceedingly complex.

The increase in uterine weight between Days 11 and 1 can be ascribed to the high rate of oestradiol secretion towards the end of the oestrous cycle (Joshi, Watson & Labhsetwar, 1973). There may be a concomitant expansion of the uterine vasculature (Bacsich & Wyburn, 1940) and this could account for the higher rates of uterine blood flow and perfusion on Day 1. In addition, the level of circulating

oestradiol at oestrus (Croix & Franchimont, 1975) may still be sufficiently high to evoke vasodilatation. It is known that the endometrial blood flow of dioestrous guinea-pigs can be augmented by treatment with oestradiol (Einer-Jensen *et al.*, 1975). That vaginal blood flow is higher at oestrus than during the luteal phase can similarly be ascribed to the effect of endogenous oestrogens. The vaginal blood flow of the ewe appears to increase following the administration of oestrone (Abrams, Caton & Bazer, 1972).

A preovulatory peak in the plasma progesterone of guinea-pigs has been demonstrated by Blatchley, Donovan & Ter Haar (1976). Although it is possible that plasma progesterone was elevated in some of the guinea-pigs examined by us on Day 1, it seems unlikely that progesterone is in any way responsible for the high rate of uterine blood flow. In the ewe, progesterone tends to limit the rise in uterine blood flow elicited by oestradiol, whilst progesterone given alone has no clearcut effect (Greiss & Anderson, 1970).

Ovarian blood flow in guinea-pigs was greatest on Day 11, when it accounted for 33% of the blood supply to the genital tract. There was, however, no detectable difference in weight between ovaries with mature follicles (Day 1) and those with mature corpora lutea (Day 11). The high rate of ovarian tissue perfusion on Day 11 is consistent with observations made in sheep during the mid-luteal phase (Niswender, Moore, Akbar, Nett & Diekman, 1975) and in pseudopregnant rabbits (Novy & Cook, 1973). In these animals, the increment in ovarian blood flow reflected the high rate of perfusion of the corpora lutea.

On Day 11 of the guinea-pig cycle there is a high level of progesterone in ovarian venous blood (Blatchley, Donovan, Horton & Poyser, 1972; Joshi *et al.*, 1973) and in the general circulation (Blatchley *et al.*, 1976). A high rate of ovarian blood flow is probably a prerequisite for the high rate of progesterone secretion. It cannot be ruled out that there is a positive feedback mechanism whereby an elevation of plasma progesterone causes an increase in ovarian blood flow but, as in the ewe (Niswender *et al.*, 1975), there may be other factors, such as LH, that regulate ovarian blood flow and thereby the rate of progesterone secretion.

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