LOCAL TRANSFER OF $^{133}\text{XENON}$ FROM THE UTERINE HORN TO THE IPSILATERAL OVARY IN THE MOUSE, HAMSTER AND GUINEA-PIG

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In the male, a countercurrent mechanism between vena and arteria spermatica interna seems well documented. The exchange has been described for heat (Waites, 1970), inert gases (Einer-Jensen, 1974a) and for testosterone (see Setchell, 1973; Einer-Jensen, 1974b).

In the female, much less evidence exists for a similar exchange between the cranial uterine and ovarian blood vessels, although the vessels are close together in many species including sheep, horses, cattle, pigs, rats, rabbits and guinea-pigs (see Goding & co-authors, 1972). So far, a local exchange has only been described with $^{133}\text{xenon}$ in sheep (Coudert, Phillips, Faiman, Chernecki & Palmer, 1974a) and with prostaglandin $\text{F}_{2\alpha}$ in sheep (McCracken, Baird & Goding, 1971; McCracken & co-authors, 1972) and cattle (Hixon & Hansel, 1974).

Using a method similar to the one indicating recirculation of the inert gases, $^{133}\text{xenon}$ and $^{85}\text{krypton}$, in the male countercurrent system (Einer-Jensen, 1974a), the present experiment was performed to investigate whether $^{133}\text{xenon}$ injected into the lumen of one uterine horn could be found in a higher concentration in the ipsilateral ovary than in the contralateral ovary.

Groups of four to eight adult mice, rats, rabbits, hamsters or guinea-pigs were used (Table 1). Of the seventy-nine animals used, twenty rats were at Day 2 of pregnancy which was initiated by caging single oestrous females overnight with two males. If spermatozoa were observed in the vaginal smear the following morning, the day was regarded as Day 1 of pregnancy. The rats, hamsters and guinea-pigs were anaesthetized with an intraperitoneal injection of 25 to 30 mg Nembutal/kg; mice were given 50 mg/kg. Rabbits were anaesthetized by giving a slow intravenous infusion of Nembutal until anaesthesia was obtained (20 to 30 mg/kg). The abdomen was opened and 0.01 to 0.1 ml $^{133}\text{xenon}$ -saline (0.5 to 2 mCi/ml, New England Nuclear) was injected through the wall into the lumen of the left uterine horn through a 26-gauge needle. After the injection, the abdominal wall was temporarily closed with wound clips. In fifteen rats and five hamsters, both tubes were ligated close to the uterotubal junction with 5-0 silk before injection. In six mice and five hamsters, the oviducts were ligated 1 week before the injection.

The abdominal wall was reopened 1, 5 or 30 min after the injection, and the

Table 1. Countercurrent exchange of $^{133}\text{xenon}$ between the blood vessels in the female genital tract after injection into the lumen of the uterus

Species	No. of animals	Reproductive state	Oviduct ligated	Time between xenon injection and autopsy (min)	Ovaries (cl/min)		Uterus (cl/min)	
					Injected side	Uninjected	Injected horn	Uninjected horn
Rat	5	Oestrous	No	5	9 ± 2.7	14 ± 4.8 N.S.	1477 ± 827.3	16 ± 8.4**
	5	Dioestrous	No	5	9 ± 1.7	11 ± 3.3 N.S.	869 ± 1482.2	42 ± 57.3 N.S.
	5	Pregnant†	Yes§	1	15 ± 16.5	10 ± 6.4 N.S.	1447 ± 1757.6	25 ± 26.3*
	5	Pregnant†	Yes§	5	11 ± 2.8	6 ± 2.8**	127 ± 78.1	20 ± 25.3*
	5	Pregnant†	Yes§	30	10 ± 7.2	7 ± 3.1 N.S.	101 ± 127.5	7 ± 4.3(*)
Mouse	6	Pregnant†	No	5	17 ± 12.4	8 ± 2.5 N.S.	268 ± 122.1	9 ± 2.3**
	5	Not known†	No	5	48 ± 23.5	18 ± 22.3*	291 ± 188.5	83 ± 113.6*
	8	Dioestrous	No	5	132 ± 49.9	12 ± 6.3**	188 ± 180.6	39 ± 59.2*
	6	Not known†	Yes¶	5	112 ± 96.3	8 ± 1.5*	699 ± 655.0	110 ± 165.1*
	5	Dioestrous	No	5	9 ± 1.0	7 ± 1.9 N.S.	617 ± 606.4	10 ± 2.4*
Rabbit	5	Not known†	No	5	102 ± 88.5	8 ± 2.0*	5365 ± 3192.9	328 ± 393.4**
	5	Not known†	Yes§	5	28 ± 29.7	9 ± 2.0(*)	550 ± 464.2	14 ± 3.1*
	5	Not known†	Yes¶	5	44 ± 38.9	10 ± 0.9*	55 ± 24.1	11 ± 4.1*
Guinea-pig	5	Not known†	No	5	15 ± 5.4	9 ± 3.3*	7557 ± 4176.3	1288 ± 2137.2**
	4	Not known†	No	5	33 ± 33.4	7 ± 1.3*	10,000 ± 2601.6	1277 ± 1807.7**

Results are stated as means ± S.D. (* = $0.05 < P < 0.1$; ** = $P < 0.05$; *** = $P < 0.01$ in t test between paired values. N.S. = not significant.

† Day 2 of pregnancy.

‡ No smear was taken.

§ Ligated immediately before injection.

¶ Ligated 1 week before injection.

ovaries and the middle third of the left and right uterine horns were removed. Each tissue was immediately placed on a separate glass slide and covered with plastic tape (Minnesota Mining Co., No. 810). All the ovaries except those of the mice were quickly separated from the tubes before covering.

The slides were placed under a shielded Geiger Muller tube (diameter 2.0 cm) and the γ -emission was counted and printed out (modified DOT instrument, EON Corp., Brooklyn, New York).

Each tissue was counted for 3 min and the results were expressed as ct/min. The counting from any one animal was finished within 15 min after the removal of the first organ.

In all three groups of mice, including the group with ligated oviducts, there was a significant increase ($P < 0.05$, Student's t test) in radioactivity in the ovary on the injected side compared to the uninjected side (Table 1).

A significantly higher group mean radioactivity ($P < 0.05$) was also seen in the hamster ovaries from the injected side in two out of three groups when compared with the ovaries from the uninjected side. In the third group, the mean radioactivity in the ovary from the injected side was three times higher than on the opposite side. In the guinea-pigs also, an increase was observed in both groups, the difference being significant ($P < 0.05$) in one.

In one group of rats pregnant on Day 5, a significant difference ($P < 0.01$) was observed between the radioactivity in the ovaries. In the other groups of rats, no difference was observed.

In rabbits, there was no indication of a difference in radioactivity between the ovaries.

Leakage of radioactivity from one uterine horn to the other was observed in some animals of all species.

These results showed that there was more radioactivity in the ovary connected with the uterine horn injected with $^{133}\text{xenon}$ -saline than in the contralateral ovary in the mouse, hamster and guinea-pig.

The results obtained in the rat were inconclusive, as there was a significant increase in one group ($P < 0.01$) after 5 min, but three other groups did not show the same increase at the same time interval. In the rat, the cranial uterine artery or nerve fibres in the wall of the blood vessel seem to be more important than the vein for transferring the local message of pregnancy from the uterus to the ovary (O'Shea & Lee, 1973), indicating that a nervous reflex may be the mediator.

If the gas was redistributed through the general circulation, the radioactivity would be the same in both ovaries. A distribution through the tube can be excluded because the difference was observed also in animals with ligated oviducts. Injection of $^{85}\text{krypton}$ -saline into a branch of the utero-ovarian vein in ewes resulted in a peak of radioactivity in the ipsilateral ovary after less than 1 min (N. Einer-Jensen and J. A. McCracken, unpublished observation). The later clearance of the gas was rapid. This finding makes a redistribution through the lymph system unlikely.

The most likely way for redistribution seems to be a countercurrent exchange of the gas from the uterine vein blood to the arterial ovarian blood in the pampiniform-like plexus formed by the vessels. A similar redistribution has

previously only been postulated for prostaglandin $F_{2\alpha}$ in the ewe (McCracken *et al.*, 1971, 1972), although doubt has been raised as to whether the mechanism is of physiological importance (Restall, Hearnshaw, Gleeson & Thorburn, 1973; Lamond & Drost, 1973) or even exists (Coudert *et al.*, 1974b). The two papers of Coudert *et al.* (1974a, b) are, however, somewhat conflicting. In the first, a transfer of ^{133}Xe from the uterine vein to the ovarian artery is described and taken to indicate a passive diffusion of the gas between the blood vessels. In the second paper, the authors state "any forms of the counter-current mechanism examined so far do not appear to be applicable to the utero-ovarian circulation". The rejection seems to be based on the anatomy of the vessels, because the authors see no structure which can be held responsible for the production of a concentration gradient although such structures have previously been described (see Goding *et al.*, 1972; Ginther & Del Campo, 1973).

The method used in the present experiment cannot quantify the effectiveness of the countercurrent exchange since xenon is a gas and can escape from the organs during handling even when the blood circulation is stopped. This is especially critical with small organs such as the ovaries. After covering the organs with the plastic tape, the decrease in radioactivity is rather slow.

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