Exchange of krypton-85 between the blood vessels of the human uterine adnexa

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Summary. A miniature Geiger–Müller probe was inserted into one ovary of 8 women undergoing hysterectomy. A control probe was inserted into the other ovary of 2 of the women. Krypton-85 in 0-15 m-NaCl was infused into the adjacent utero-ovarian vein and the radioactivity was registered for 5–14 min after the infusion. An increase of radioactivity was recorded in the ovary in 5 cases. In one of the women with 2 probes, no increase in radioactivity was observed in the control ovary. The results show a local transfer of gas from the ovarian branch of the uterine vein into the adjacent ovary, which may be due to a countercurrent exchange mechanism between the vessels of the human uterine adnexa.

Introduction

In several mammalian species an intimate anatomical relationship between the ovarian artery and the utero-ovarian vein has been demonstrated (Barrett et al., 1971; McCracken, 1972; McCracken et al., 1972; Del Campo & Ginther, 1972, 1973; Vollmerhaus, 1964). The functional significance of this vascular construction is unclear. In the sheep, experimental evidence supports the view that prostaglandin (PG) F-2α of uterine origin causes luteal regression (McCracken et al., 1972), and that a high local concentration of PGF-2α in the ovary is made possible by transfer of the substance from the utero-ovarian vein to the ovarian artery. This would prevent PGF-2α from being rapidly decomposed in other organs (Piper, Vane & Wyllie, 1970).

Functional evidence for a countercurrent transfer of PGF-2α in the ovarian pedicle of the sheep was provided by McCracken et al. (1972) who observed that tritium-labelled PGF-2α infused into the uterine vein appeared in higher concentrations in the ovarian artery than in aortic blood collected simultaneously. Studies in cattle gave further evidence for a local transfer; instillation of unlabelled PGF-2α into the uterine cavity resulted in a higher concentration of this prostaglandin in the ovarian artery than in the carotid artery (Hixon & Hansel, 1974).

Inert radioactive gases have also been used in attempts to demonstrate a countercurrent exchange mechanism. Infusion of xenon-133 into one uterine horn of the mouse, hamster and guinea-pig was followed by higher concentrations in the adjacent than in the opposite ovary (Einer-Jensen, 1974). A transfer of krypton-85 from the utero-ovarian vein to the ipsilateral ovary in the sheep has been demonstrated by using miniaturized Geiger-Müller probes inserted into both ovaries (Einer-Jensen & McCracken, 1977).

Recent studies in women (Bendz, 1977) have demonstrated a close anatomical relationship between the tortuous ovarian artery and the utero-ovarian vein. The vascular arrangement is very similar to that found in the sheep and the purpose of the present study was to investigate whether an indicator substance such as krypton-85 can be transferred from the utero-ovarian vein to the adjacent ovary of women.
Materials and Methods

The study was approved by the local ethical committee. Women who were admitted to the hospital for hysterectomy because of uterine fibroids were given detailed information about the study and were asked if they were willing to participate: 12 agreed. No post-operative complications were observed.

For technical reasons 4 women were omitted from the study. These patients had large uterine fibroids which made the adnexa inaccessible. Data about the remaining 8 patients studied are presented in Table 1.

**Table 1. Clinical data on the patients studied**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Day of cycle</th>
<th>Ovary with probe*</th>
<th>Operation</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>4</td>
<td>L</td>
<td>Hysterectomy + right adnexectomy + left tubal resection</td>
<td>Chronic tubal infection + adhesions</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>7</td>
<td>R</td>
<td>Hysterectomy</td>
<td>Adnexal vasculature normal</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>8</td>
<td>R + L</td>
<td>Hysterectomy + left adnexectomy</td>
<td>Small ovarian cyst left side, adnexal vasculature normal</td>
</tr>
<tr>
<td>4</td>
<td>41</td>
<td>9</td>
<td>R + L</td>
<td>Hysterectomy</td>
<td>Adnexal vasculature normal</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>22</td>
<td>L</td>
<td>Hysterectomy + right adnexectomy</td>
<td>Right ovarian cyst, left adnexal vasculature normal</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>22</td>
<td>L</td>
<td>Hysterectomy + right adnexectomy</td>
<td>Right ovarian cyst, left adnexal vasculature normal</td>
</tr>
<tr>
<td>7</td>
<td>45</td>
<td>26</td>
<td>R</td>
<td>Hysterectomy</td>
<td>Adnexal vasculature normal</td>
</tr>
<tr>
<td>8</td>
<td>42</td>
<td>27</td>
<td>R</td>
<td>Hysterectomy</td>
<td>Adnexal vasculature normal</td>
</tr>
</tbody>
</table>

* L = left, R = right.

Operative procedure

The patients were premedicated with meperidine hydrochloride, promethazine chloride and atropine sulphate in doses according to age and body weight, 1 h before anaesthesia. Induction was made with thiopentone, given i.v., followed by succinylcholine chloride for tracheal intubation. Anaesthesia was maintained with nitrous oxide–oxygen and small doses of meperidine hydrochloride. The patients were curarized with alcuronium chloride and ventilated by means of a non-rebreathing system.

The abdomen was opened by a low mid-line incision and the intestines were pushed upwards with the aid of abdominal swabs. The uterus was fixed ventrally by sutures tied to a self-retaining abdominal retractor. The distal portions of the Fallopian tubes were gently grasped with Babcock clamps which were fixed to the retractor.

A uterine vein running towards the ovarian pedicle was selected for infusion of krypton-85 and punctured with a pointed Teflon cannula (o.d. 1 mm). In most cases, a vein with a visible tortuous artery on the surface could be chosen for puncture (Text-fig. 1). Sometimes a uterine vein was inaccessible in the parametrium due to the large size of the uterus or to fibrous adhesions and then a vein in the ovarian pedicle was used.

Procedure for measurements

The krypton-85 (sp. act. 3–5 mCi/ml) was obtained from New England Nuclear (U.S.A.) and 400 µCi were dissolved in 5 ml 0.15 M NaCl. For all attempts except one (Patient 5) this amount of krypton was divided into two equal doses, permitting a change of site of injection or probe if no counts could be detected during the first infusion period. A 1–3 min infusion of krypton-85 was carried out from a hand-held syringe or (in Patient 2) by an infusion pump. The cannula was then flushed with physiological saline.
Miniaturized Geiger–Müller probes (specially manufactured by Dosimeter Ltd, Cincinatti, U.S.A.), length 8 mm, diameter 1.5 mm, and their flexes (length 60 cm) were sterilized in 70% ethanol for 3–12 h. The probes were easily destroyed by mechanical stress and if the connecting plug of the flex was immersed in the disinfectant, no counts were obtained until the connecting plug had been allowed to dry for 3–18 h.

A metal rod with a diameter of 1.5 mm was passed into the ovary and withdrawn. The Geiger–Müller probe was then inserted into the tunnel made by the rod. When a corpus luteum was present (Patients 5 and 7) the tunnel was made in the corpus luteum, avoiding the central cavity; otherwise placement was in the ovarian stroma, carefully avoiding any big follicles. The procedure was repeated on the opposite side in Patients 3 and 4. The flexes of the probes were fixed to the retractor.

The wall thickness of the cylindrical stainless-steel window of the probe is stated to be 29 mg/cm², which according to the producer will permit penetration of 50% of the β-emission from the krypton-85. Because the predominating emission from krypton-85 is of the β type, the amount of tissue from which registration of radioactivity is possible is an approximately 0.5 mm thick layer around the detector. Only a small fraction of the total radioactivity reaching the ovary was therefore detectable.

The radioactivity measured by the probes was registered on two modified ratemeters intended for use in the diagnosis of ocular tumours (Dosimeter Ltd, Cincinatti, U.S.A.). A print-out of the registered counts was made, up to a maximum of 14 min after the infusion of the krypton-85.

**Results**

In 5 of the 8 patients (Nos 2, 3, 4, 5 and 7), in which functioning probes were inserted into the ovaries and krypton-85 could be infused i.v., there was an ipsilateral increase in the ovarian radioactivity within 60 sec (Text-figs 2a–e). The maximum radioactivity (range 65–1760 c.p.m.) was registered 2–4 min after the start of the infusion. The radioactivity decreased to 21–550 c.p.m. 3–12 min after registration of maximal counts. The background radioactivity level was 0–40 c.p.m.
Text-fig. 2. Counts registered in the ipsilateral ovaries (a, b, c) and both ovaries (d, e; —— ipsilateral, ---- contralateral) of women after a 1–3 min infusion (between double arrows) of krypton-85 (200 µCi in 2–5 ml saline in (a), (c), (d) and (e); 400 µCi in 5 ml saline in (b)). The probe was inserted into a corpus luteum in (b) and (c). np = new probe inserted; pm = probe moved; pof = probe out of function; pr = probe removed.

In Patient 3 who had probes in both ovaries, the radioactivity in the contralateral ovary remained at the background level (below 10 c.p.m.) during and after the $^{85}$Kr infusion (Text-fig. 2d). In Patient 4, also with bilateral probes, the tortuous artery on the surface of the punctured vein was accidentally cut off by the cannula and haematoma compressing the vein was formed. When $^{85}$Kr was injected, there was a more pronounced increase in the radioactivity of the contralateral than the ipsilateral ovary (192 versus 65 c.p.m.) (Text-fig. 2e). The maximum radioactivity was recorded on both sides 1 min after the infusion was finished. The direction of flow in the punctured vein was not observed.

No significant increase in radioactivity could be detected in Patients 1, 6 and 8. In Patient 8 the direction of flow in the punctured vein was towards the uterus. In Patients 1 and 6 leakage of blood and formation of haematomata around the punctured veins were observed.

**Discussion**

In 5 of the 8 subjects studied, krypton-85 reached the ovary when infused into the adjacent uterine vein. The results are compatible with the hypothesis that a countercurrent exchange may exist between the blood vessels in the human uterine adnexa.
In one of the two subjects with probes inserted into both ovaries, the radioactivity of the contralateral ovary remained at the background level after the infusion of krypton-85, indicating that recirculation via the systemic circulation could not explain the observed distribution to the ipsilateral ovary (Text-fig. 2d). This agrees with earlier observations that only a small fraction of krypton-85 remains in the blood of human beings after one passage through the lungs (Chidsey, Frits, Hardevig, Richards & Courrand, 1959). The comparatively lower peak in the ipsilateral ovary of the Patient 4 may have been due to a reduced arterial supply caused by the accidental damage of a main arterial branch (Text-fig. 2e). Since the radioactivity in the contralateral ovary was rather high, it is unlikely that the distribution of krypton-85 to that ovary occurred via the systemic circulation. A more probable explanation would be a change of the direction of blood flow in the utero-ovarian veins, resulting in a transfer from the ipsilateral veins to the corresponding vessels on the other side. Such a retrograde venous flow was observed in Patient 8 for whom no counts were recorded in the ipsilateral ovary, indicating that $^{85}$Kr does not back up the venous vessels to the ovary. This change of flow could be due to a number of factors such as traction of the uterus or the ovary during cannulation and infusion, disturbance by swabs packed around the uterus, pathological changes as uterine fibroids, chronic pelvic inflammatory disease or ovarian cysts. In the 2 women in which the vein was damaged (Patients 1 and 6), no exchange to the ipsilateral ovary was expected after the injection of $^{85}$Kr into the myometrium because of the redistributed venous flow. It is thus obvious that a number of variables of technical, anatomical and pathological nature may influence the results, and it is sometimes difficult to tell how representative are the observed findings of the normal state. It is, of course, impossible to perform experiments of this kind on women with no pathological changes in the reproductive tract. However, as indicated in Table 1, the vasculature appeared macroscopically normal in both adnexa of 5 patients and in one of the adnexa of each of 2 patients.

The results of the present study are very similar to those found in the sheep with a comparable technique (Einer-Jensen & McCracken, 1977). The transfer of the $^{85}$Kr is probably based on passive diffusion aided by the close relationship between the vein and the tortuous artery. A simple diffusion from the vein to the ovary is very unlikely since the distance between the site of venous infusion of $^{85}$Kr and the ovary was in all cases more than 3 cm. One possibility to investigate this matter further would be to clamp off the ovarian artery before infusion, as was done in the sheep by Einer-Jensen & McCracken (1977). However, the transfer of an inert gas does not necessarily indicate a countercurrent exchange of physiologically active substances. The normal ovarian cyclic functions in women are probably not dependent on the presence of the uterus or the Fallopian tube (Stewart, 1973; Janson & Jansson, 1977), but a countercurrent mechanism may participate in intra-ovarian regulatory functions of a short-loop feedback type. If, for instance, ovarian steroids are transferred from the vein to the artery the altered ovarian steroid environment would unilaterally modulate the ovarian sensitivity to gonadotrophins (Judd, 1978).

Experiments are in progress to test whether a countercurrent transfer of steroids can occur in the ovarian pedicle of women, as has been shown for sheep (McCracken & Einer-Jensen, 1976).

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References


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