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Mammalian oviduct vasculature and blood flow

Vascularización y flujo sanguíneo del oviducto en mamíferos

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The anatomy of the arterial and venous vessels of the mammalian oviduct is well described in women and in laboratory and farm animals. The arteries are derived from the ovarian and uterine stems; the relative contribution of these vessels, however, or variations in that contribution with the menstrual or estrus cycle and/or gamete or embryo transport is unknown. The venous drainage varies between species with either utero-ovarian or ovarian venous drainage. Evidence of the counter-current exchange of ovarian steroids between the ovarian venous drainage and the ovarian artery suggests a capacity for local interactive regulation of uterine, tubal and ovarian function.

Determination of rabbit oviduct microvascular architecture (MVA), using the corrosion vascular cast - scanning electron microscope technique, has revealed that oviduct MVA varies along the length of the tube. The predominant differences are in the subserosal and submucosal MVA. Isthmic subserosal MVA is characterised by an extensive interlocking venous plexus; venous distension of this plexus 12 hours after ovulation is observed to resolve 36 hours after ovulation and implies a potential to limit isthmic ovum or embryo transport. Isthmic plicae are well supplied with arterioles which branch terminally, high in the plical core; this contrasts with ampullary plical MVA in which the submucosal capillaries drain to large venules which originate high in the mucosal fold. These observations suggest a greater blood flow capacity to the isthmic submucosal capillaries and a greater venous drainage capacity in the ampulla; consequently a pattern of intraluminal tubal fluid movement may be initiated or an existing pattern modified.

Rabbit oviduct MVA was also examined after oophorectomy and during pregnancy; the morphological changes suggest a sensitivity to ovarian and pregnancy steroids and/or peptides. The variations in rabbit oviduct MVA, vascular perfusability and macromolecular permeability have been documented in the experimental hydrosalpinx. In addition, MVA changes associated with tubal ligation and microsurgery have been studied and the results described in the text. Furthermore, future directions in oviduct microvascular research are outlined.

INTRODUCTION

Mammalian oviduct vascular anatomy is well described in women, laboratory and farm animals and will not, therefore, now be described in great detail. The tubal arteries are derived from branches of the ovarian and uterine arteries, not withstanding extensive connections (Warwick and Williams, 1973; Watanabe, 1963), the relative contribution of these vessels or the variation in that contribution with the menstrual cycle in women or the estrus cycle in laboratory or farm animals or during mammalian ovum or embryo transport is largely unknown. The venous drainage is described as being related to the arteries of supply; cyclical variation, if any, is yet to be determined.

Human oviduct vasoulature

Branches of the uterine artery, in the human oviduct, in general, supply the isthmus and branches of the ovarian artery the remaining parts of the tube. Either artery alone however, may supply the whole tube (Eddy and Pauerstein, 1980). Borell and Fernstrom (1953), using an arteriographic technique, demonstrated this in vivo and described women where the tubal arterial supply is derived entirely from either the ovarian or the uterine arteries or from an admixture of the two. This series, however, was small and the observations were not related to any specific time in the menstrual cycle.

The venous drainage follows that of the arterial supply (Eddy and Pauerstein,

1980). Tubal venous drainage in the ovarian vein is particularly significant as the ovarian vein and artery are closely related in the human ovarian pedicle (Bendz, 1977; Bendz and Hansson, 1982a). Areas of contact between the ovarian artery (Blancardi, 1987; Bendz *et al.*, 1982a) and vein are characterised by thinning of the ovarian vein wall (Bendz, 1977; Bendz *et al.*, 1982a). This anatomical arrangement is consistent with the hypothesis that there is a counter current transfer of factors from ovarian veins to artery (Bendz, 1977; Bendz and Hansson, 1982; Bendz *et al.*, 1982a; Hunter *et al.*, 1983).

Human oviduct microvasculature

Human Fallopian tube microvasculature was studied in 200 *post mortem* specimens injected with china ink and gelatin; the tubes were cleared and examined by stereo and light microscopy. The following description is based on the reports of Gillet and Leissner, 1967; Gillet and Koritke, 1967; Koritke and Gillet, 1967; Koritke *et al.*, 1968a and b; Müller *et al.*, 1968. The tubal subserosa is supplied by arterioles which arise from a juxta-tubal arterial arcade. The myosalpinx is supplied by tortuous arteries which subsequently pass through it to give rise to the mucosal arterioles. These are located at regular intervals of 0.3 - 1.5 mm, are coiled and terminate in a dense submucosal capillary network; this network subsequently drains to irregular calibre venules which pass, parallel to each other and at right angles to the long axis of a mucosal fold, to join deeper venules. Fimbrial microvascular architecture (MVA) differs from that of the isthmic or ampullary mucosa in that arteries are more numerous and are located peripherally around a centrally located fimbrial core venule. Tubal mucosal vasculature varies with the menstrual cycle; during the proliferative phase mucosal arterioles become increasing coiled and this progresses, during the secretory phase, to a maximum at the time of menstruation. These vascular changes are most pronounced in the fimbria. Mucosal venules are markedly dilated at the time of ovulation and maximally dilated at the time of menstruation. Mucosal venule diameters range from 75 um in the proliferative phase to 175 um premenstrually and 120 um at the time of menstruation. Mucosal arteriolar coils progressively tighten during pregnancy. After the menopause, mucosal arterioles and venules are dilated and the mucosal arterioles are less tightly coiled. Mucosal capillaries are normally 10 um in diameter; premenstrually capillary diameters increase to 20-25 um. These morphological studies, led to the conclusion that human tubal microvasculature varies with the menstrual cycle, pregnancy and after the menopause; this was interpreted to imply a sensitivity of the tubal vasculature to ovarian and pregnancy hormones. The implications and the significance of the observations were not further discussed; that the studies were of *post mortem* Fallopian tubes makes *in vivo* interpretation difficult. One other study examined human tubal microvasculature and many blood vessels in the tube, particularly in the fimbria, were described (Hayashi, 1973).

Rabbit oviduct vasculature

Rabbit tubal vasculature has been studied by Robinson (1903), Barcroft and Rothschild (1932), Gothlind and Carter (1969), Del Campo and Ginther (1972) and Dickson *et al.* (1974), and, in general, their descriptions are similar.

The ovarian arteries originate from the abdominal aorta and, as they pass caudally, give rise to a long caudal branch which runs about 2 cm from and essentially parallel to the tube. This caudal branch supplies the tube and the tip of the uterine horn. The cranial branch of the ovarian artery divides into a branch which supplies the ovary and a branch which supplies the ampulla and surrounding tissues; in addition, the ovarian branch divides as it approaches the ovary and some of the branches supply the tube. The uterine arteries arise from a branch of the internal iliac arteries and pass ventral toward the cranial portion of the vagina and cervix

to run parallel to the caudal portion of the uterine horn and then divide into two prominent branches. The medial branch supplies the caudal portion of the uterine horn and ends by anastomosis with the contralateral uterine artery. The lateral branch provides a number of branches which supply the cranial half of the uterine horn and the tube. The main oviductal branch of the ovarian artery merges with the cranial branch of the uterine artery in what Robinson (1903), termed the genital "vascular circle". Dickson *et al.* (1974), also described anastomoses between branches of the ovarian and uterine arteries within the web of the oviduct-uterine arcade. In addition, they reported oviductal ramifications of the ovarian branch of the ovarian artery which anastomose on the ampullary surface with the cranial terminal ramifications of the oviductal branch forming a smaller oviductal vascular circle similarly described by Robinson (1903).

The anatomy of the venous system is similar to that of the corresponding arteries. The right ovarian vein empties into the vena cava and the left into the lumbar vein (Del Campo and Ginther, 1972; Dickson *et al.*, 1974).

Rabbit oviduct microvasculature

Estrus rabbit oviduct MVA has been determined by using the corrosion vascular cast - scanning electron microscope (SEM) technique. This technique facilitates the easy differentiation between arterioles and venules in the three dimensional examination of the MVA (Verco *et al.*, 1983a). Vascular corrosion casts reveal the perfused microcirculation at the time of casting and the technique compares favourably with osmium tetroxide vascular perfusion fixation which is not associated with the tissue distortion that usually occurs with primary aldehyde fixation (Verco *et al.*, 1983a).

Rabbits are anaesthetized, the great vessels cannulated and the blood washed from the vasculature in this technique. After blood washout the vasculature is perfused with the casting medium, prepolymerized methylmethacrylate, which is allowed to polymerize under slight positive intravascular pressure. The tissue is digested from the casts with KOH and the casts cleaned gently in an ultrasonic bath.

The resultant casts, which could be dissected or freeze cut, were examined by stereomicroscopy, scanning electron microscopy and by the stereoscopic examination of SEM photomicrographs with 5 degree tilt separation.

The casts obtained are readily identifiable as oviducts in which the isthmus, ampullary-isthmic junction (AIJ), ampulla and fimbria are clearly recognized.

Examination of the oviduct vascular casts revealed that the MVA varies characteristically along the length of the tube. The major differences are in the subserosal and submucosal microvasculature.

There is an extensive interlocking venous plexus in the isthmic subserosa; ampullary subserosal vasculature, in contrast, is comprised of parallel branching arteries and veins. Isthmic plicae are well supplied with arterioles which branch little before terminal ramification, into capillaries, high in the plical core. Isthmic plical capillaries drain either down the fold or directly to centrally located plical core venules. Ampullary plical arterioles are less frequently observed and either branch low in a mucosal fold or pass to the top of a fold, along which they run before terminal ramification into capillaries. Ampullary plical capillaries drain to large venules that originate high in the plical core. Fimbrial arterioles and venules exhibit parallel branching; near the edge of a fimbrial fold the arterioles branch terminally into capillaries which drain to the large, accompanying and frequently observed core venules (Verco *et al.*, 1983a).

These studies suggest, firstly, that isthmic subserosal venous plexus dilatation (caused by either a rise in venous pressure or a fall in venous wall smooth-muscle tone) could, within the limiting perimeter of the serosal connective tissue, occlude the isthmic lumen to ovum or embryo transport. Secondly, the observed differences in the MVA imply a greater blood delivery to the submucosal capillary network of the isthmus and a greater venous

drainage capacity in the ampulla. This suggests that there may be a net movement of intravascular fluid to the interstitium and possibly thence to the tubal lumen in the isthmus, and a net movement of tubal fluid from the tubal lumen to the mucosal interstitium and thence to the subepithelial capillaries in the ampulla (Verco *et al.*, 1983a). A pattern of tubal luminal fluid movement may thus be initiated or a preexisting pattern of fluid flow along the tube modified. This is consistent with the isthmic to ampullary luminal fluid current described by Black and Asdell (1958) and Koester (1970).

Rabbit oviduct MVA after oophorectomy and in mid pregnancy

Four weeks after bilateral oophorectomy tubal microvascular connections were unaltered; when compared with control oviducts there is a decrease in the frequency and size of the large ampullary plical and fimbrial core venules and, in addition, fimbrial subepithelial capillary density is reduced (Verco *et al.*, 1983b).

Oviduct MVA in rabbits 2-3 weeks pregnant is characterised by venous distension in the isthmic and ampullary subserosal veins and in the fimbrial core veins when compared with control rabbit oviduct MVA (Verco *et al.*, 1984a).

Observations of rabbit oviduct MVA after oophorectomy and during pregnancy suggest a sensitivity and perhaps even the dependence of the tubal vasculature on local or circulating ovarian, embryonic or placental hormones (Verco *et al.*, 1983a, 1984b). Tubal MVA may, thus, vary at the time of ovulation and tubal gamete or embryo transport; such tubal MVA variations could be focal, regional or involve all the tubal MVA.

Rabbit oviduct MVA 12 and 35 hours after ovulation

To delineate further the role of the tubal MVA at the time of ovulation and tubal ovum transport, corrosion vascular casts were prepared 24 and 48 hours after intravenous HCG injection to induce ovulation (Verco *et al.*, 1984b). Ovulation occurs some 10 to 14 hours after HCG injection in rabbits (Harper, 1963); ova would be at the AIJ 24 hours and traversing the isthmus 48 hours after HCG, injection (Pauerstein *et al.*, 1974). Isthmic subserosal venous plexus dilatation is greater at 24 hours than either at 48 hours after HCG or in controls. Isthmic subserosal venous plexus dilatation at 48 hours is less than that at 24 hours after HCG and is similar to that observed in controls. Isthmic luminal space in some tubal casts and in all tubal tissue segments after fixation by vascular perfusion with osmium tetroxide are of a similar area which is greater than that observed in controls (Verco *et al.*, 1984b). Isthmic subserosal venous plexus distension did not maintain isthmic luminal occlusion, as might have been expected. It is possible that the patchy nature of increased tubal luminal area reflects tubal segments with closely adjacent ova; further examination by serial section may be warranted. However, in the absence of any other consistent explanation for the pre-isthmic delay in ovum transport, it is reasonable to still speculate that dilatation of the isthmic subserosal venous plexus limits isthmic wall distensibility and thus contributes to the known pre-isthmic delay in ovum transport.

Westman (1937) reviewed his earlier observations in rabbits and rhesus monkeys and indicated that the fimbria are engorged with blood at the time of ovulation; similar observations, in pigs and sheep have been reported by Hunter (1982). Fimbrial "erection", aiding ovum capture, was a widespread concept, however. Andersen (1927) considered that the wide vascular spaces in the tubal mucosal folds were lymphatics with good drainage and that mucosal "erection" was impossible.

There is no evidence, from the MVA studies, despite fimbrial core venous distension, of fimbrial "erection". However, the casts prepared at 24 hours after HCG injection are prepared at least 10 hours after ovum capture and therefore observation at the time of ovulation is required to determine the accuracy or inaccuracy of this suggested role for the fimbria.

Rabbit oviduct MVA capillary perfusion and macromolecular permeability in the mechanically induced hydrosalpinx

Hydrosalpinges were induced by isthmic and ampullary occlusion with small tantalum clips (Verco *et al.*, 1982; Verco and Gannon, 1984 and 1985). The resultant corrosion vascular casts exhibit isthmic and ampullary luminal dilatation, reduction in the extent of projection of the primary mucosal fold MVA into the lumen, and loss of secondary mucosal fold MVA. Plical MVA is preserved; in contrast, interplical subepithelial capillaries are not cast. Larger and more extensively branching interplical subepithelial arterioles are observed in both the isthmus and the ampulla. Isthmic and ampullary subserosal venous distension is greater in the hydrosalpinx than in controls or in adjacent tubal segments. The reduction in interplical subepithelial cast filling indicates poor perfusion in this region at the time of casting. Subepithelial capillary perfusability and permeability to native rabbit and bovine serum albumin are reduced in the hydrosalpinx, particularly between plicae. Poor interplical subepithelial capillary perfusion is probably the underlying mechanism of interplical deciliation, previously reported in this model (Vásquez *et al.*, 1981; Kleinstein *et al.*, 1982).

Preservation of the plical MVA, the absence of interplical subepithelial capillary filling, and reduced interplical subepithelial capillary perfusion indicate, since all mucosal subepithelial capillaries are exposed to the same increased tubal intraluminal hydrostatic pressure, that the microvascular changes are primarily due to stretching of the tubal wall. The larger and more extensive mucosal arterioles of the hydrosalpinx suggest increased blood pressure in the hydrosalpinx; in addition, the subserosal venous dilatation observed in the hydrosalpinx implies superregulation of blood flow and thus increased blood flow in the hydrosalpinx. A net increase in capillary fluid outflow and a net decrease in capillary fluid absorption would therefore be predicted. Interstitial fluid in the hydrosalpinx could pass between the epithelial cells through "leaky" tight intercellular junctions which are rendered more "leaky" by streching of the epithelium. The reduction in subepithelial capillary permeability to albumin, in the hydrosalpinx model, would decrease osmotically driven absorption of luminal fluid. Taken together, increased hydrosalpinx blood pressure and blood flow, reduced subepithelial capillary perfusion and macromolecular permeability would result in an increase in mucosal interstitial fluid, an increase in epithelial transudation, a reduction in osmotically driven transepithelial luminal fluid absorption and reduced subepithelial capillary fluid absorption (Zweifach, 1977). Thus in this model these mechanisms would explain the maintenance of the hydrosalpinx. Reduced human fertility after salpingoneostomy for hydrosalpinges may be due to persistence of the vascular changes similar to those described above.

Rabbit oviduct MVA after Pomeroy tubal ligation and tubal microsurgery

To determine alterations in tubal vasculature after sterilization rabbit tubal MVA was examined by the corrosion vascular cast SEM technique four weeks after midisthmic Pomeroy tubal ligation (Verco *et al.*, 1983c). Tubal MVA, except within one millimeter of the site of tubal ligation, is similar to that observed in controls. The site of ligation was characterized by a randomly oriented vascular proliferation of fine vessels. This was interpreted as indicating the extent of proliferative tissue reaction to the surgery involved in tubal ligation. Pomeroy tubal ligation would be expected to have little effect on tubal, ovarian, or uterine vascular interrelationships.

Tubal MVA was examined in rabbits four weeks after transection and microsurgical anastomosis of the isthmus and the ampulla. Tubal morphology, except within 1 mm of the site of isthmic and within 150 microns of the site of ampullary anastomosis, is similar to that in control oviducts. The site of isthmic anastomosis

is characterized by a serosal vascular proliferation (Verco *et al.*, 1985); this indicates the local tissue hyperplasia reported following isthmic anastomosis (Halbert *et al.*, 1981; Bernhardt-Huth *et al.*, 1981). The site of ampullary anastomosis has little serosal "reaction" (Patton and Halbert, 1979); transanastomotic interplical transluminal vascular bands were observed (Verco *et al.*, 1985). The vascular components of tubal function (except at and adjacent to the site of anastomosis) would vary little as a consequence of tubal microsurgery (Verco *et al.*, 1985). It is possible for tubal ovum transport to be delayed at the site of isthmic or ampullary anastomosis; in the isthmus, delay could be attributed to extraluminal restriction of isthmic distensibility and in the ampulla, to intraluminal adhesions limiting luminal diameter and distensibility. Delay in tubal embryo transport may result in embryonic degeneration in pigs (Murray *et al.*, 1971) and in rabbits (Adams, 1958); these data suggest an explanation of the reduction in nidation index after tubal surgery. The sites of isthmic and ampullary anastomosis could be loci for ectopic gestation; this is uncommon, however, in women and has not been reported in animal studies.

Ovarian venous to ovarian artery counter current exchange

The proximity of the utero-ovarian vein and the ovarian artery, in sheep, resulted in the demonstration of the counter current transfer of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), the luteolysin in sheep, from the utero-ovarian vein to the ovarian artery and hence to the ovary (Barret *et al.*, 1971; Goding *et al.*, 1972; McCraken *et al.*, 1972). Coudert *et al.* (1974a and b) disputed that the local or counter current transfer of $PGF_{2\alpha}$ occurred. Lee and O'Shea (1976) suggested that the morphological proximity of ovarian venous and arterial vessels, in opossums, implied specialization for counter current exchange. The human ovarian artery and vein are in close contact and where the ovarian artery is in contact with ovarian veins thinning of the vein wall has been reported (Bendz, 1977; Bendz *et al.*, 1982a) and the potential for counter current exchange suggested.

A local transfer mechanism, for radioactive xenon (^{133}Xe), from the uterine horn to the ipsilateral ovary has been described in the mouse, hamster and guinea pig, but not in the rabbit (Einer-Jensen, 1974). This was not observed in the rabbit where the ovarian artery, clearly, is not in close proximity to the uterine vein (Del Campo and Ginther, 1972; Ginther, 1974; Ginther, 1976; Janson and Svendson, 1975). The counter current transfer of radioactive Krypton (^{85}Kr) from utero-ovarian vein to ovarian artery and hence to the ipsilateral tube and ovary was reported in sheep (Einer-Jensen and McCraken, 1977) and, *in vivo*, in women (Bendz *et al.*, 1979). These observations supported, but did not prove the hypothesis that there is ovarian vein to artery counter current transfer of bioactive substances. The counter current transfer of progesterone (molecular weight 318) in the sheep utero-ovarian pedicle was first reported briefly by McCraken and Einer-Jensen (1976); this was later confirmed by Walsh *et al.* (1979). Subsequently Kryzmowski *et al.* (1981) demonstrated the venous to arterial counter current transfer of ^{3}H-testosterone in the vascular pedicle of the sow ovary. Kotwica *et al.* (1981), in addition, reported a counter current multiplier effect for ^{3}H-testosterone transfer from utero-ovarian vein to artery in the cow. Bendz *et al.* (1982b) demonstrated that, *in vitro*, there is a counter current transfer of progesterone and antipyrine between the human ovarian veins and the ovarian artery in the ovarian pedicle. Albumin is not exchanged which suggests that macromolecules do not freely pass across these vessel walls. Kryzmowski *et al.* (1982a), in the pig, reported the counter current exchange, between utero-ovarian vein and ovarian artery, of ^{3}H-testosterone, ^{3}H-progesterone and ^{3}H-oestradiol; radioactivity was detected in ovarian arterial blood and in the ovary. There was no contamination with blood as ^{51}Cr labelled red cells did not cross from vein to artery. Hunter *et al.* (1983)

similarly, in pigs, reported the counter current transfer of steroids and $PGF_{2\alpha}$ and speculated that, by this mechanism, isthmic function and therefore sperm transport may be facilitated. The existence of ovarian vein to artery counter current exchange would enable the local regulation of uterine, tubal and ovarian function with genital organs exposed to ovarian hormone levels higher than the peripheral hormone concentrations (Kryzmowski *et al.*, 1982b; Bendz *et al.*, 1982b).

Such an exchange mechanism renders quantification of ovarian steroids in peripheral blood interesting, but of little value in determining the genital end-organ effect. Counter current exchange between ovarian vein and artery and perhaps between ovarian and tubal lymphatics and the ovarian vessels is of particular relevance to the study of tubal vasculature. The absorption of bioactive tubal factors which could be readily transmitted by this method to the ovary may, thereby, signal, for example, the stage of embryo development.

This counter current mechanism, furthermore, may explain the generally reduced fertility in women with endometriosis and why some women with minimal or mild endometriosis are infertile (Anonymous, 1980; Thomas and Cooke 1987; West 1990). One may speculate that women with endometriosis have different venous vascular connections. Those with large endometriotic foci near the ovarian venous drainage will, but virtue of the ovarian vein to artery counter current exchange of the many biochemical products of endometriosis, have a tube and ovary which "see" these products in much higher than circulating levels and, thus, may exhibit altered function sufficient to be manifest as infertility. Thus, similarly located and similarly extensive endometriotic deposits may, depending on the venous drainage of their location, have a different effect in different women.

Similarly, vascular absorption of peritoneal fluid in women with endometriosis (Suginami *et al.* 1986), may, in the same manner, impact on the fertility of women with (mild) endometriosis.

Rabbit oviduct blood flow

Rabbit tubal vasculature may, *in vitro*, be perfused through either the uterine or ovarian arteries; *in vivo*, however, estrus rabbit tubal blood flow is derived, entirely, from the ovarian artery (Dickson *et al.*, 1974). Dickson *et al.* (1974) used the hydrogen desaturation technique to measure tubal blood flow; either hooked platinum electrodes were placed through the serosa or flat electrodes were placed on the myosalpinx just under the serosa. They observed mid-tubal blood flow as an indicator of the major vessel of supply; mid-tubal capillary blood flow was estimated at 0.584 ± 0.182 ml/min/g (Dickson *et al.*, 1974). Blasco *et al.* (1975) reported that 0.18% of the rabbit cardiac output is directed to the oviduct; this could be compared with brain and kidney blood flow being 1% and 21% of cardiac output Blasco *et al.* (1975) used radioactive microspheres to measure tubal (site not specified) blood flow; blood flow to the oviduct rises from (approximately, as it comes from a histogram) 1.5 ml/min/g in estrus rabbits to 5 ml/min/g 7 hours after HCG injection. Oviduct blood flow for the whole oviduct, rises from 0.57 ml/min/oviduct in the estrus rabbit to 1.1 ml/min/oviduct 7 hours after HCG injection (Blasco *et al.*, 1975). Waldhalm and Dickson (1976) examined rabbit oviduct mid-isthmic blood flow in the early pregnant and pseudopregnant rabbit; again platinum electrodes were implanted to measure hydrogen gas desaturation.

These electrodes were implanted in the isthmus some 2 cm from the utero-tubal junction; they suggested that "the observer must assume the site chosen is representative of the entire homogenous organ" (Waldhalm & Dickson, 1976). Estrus isthmic blood flow is 0.810 ± 0.287 ml/min/g and rises to a maximum of 1.323 ± 0.424 ml/min/g on post-coital day 4 (Waldhalm & Dickson, 1976). Subsequently studies of rabbit oviduct MVA (Verco, 1986) suggest substantial regional differences and thus it is unrealistic now to accept the proposition that tubal blood flow is homogeneous. In addition, of

course, these studies may not necessarily have observed submucosal blood flow which determines the subepithelial capillary bed capacity to be either a net fluid losing or net fluid absorbing network. The studies do, however, support the contention of Verco *et al.* (1983a and 1984b), that increased isthmic blood flow after ovulation results in a circum-isthmic sphincter preventing tubal ovum/embryo transport.

Current studies of human endometrial blood flow measurement using laser doppler flowmetry (which measures red cell flux) reveal considerable minute to minute blood flow variation ranging from 0.5 - 1.2 ml/min/g (Carati, Gannon and Verco, 1990 unpublished observations). A small number of fimbrial blood flow estimations, by this group, at the time of laparoscopy reveal flow rates ranging from 0.60 - 1.2 ml/min/g; these few observations are of a similar order of magnitude to those reported above even though CO_2, a vasodilator, is used for abdominal distension.

The techniques of transvaginal pulsed doppler blood flow velocity assessment may facilitate further understanding of tubal and ovarian arterial and venous blood flow and have already been applied to ovarian and uterine arterial blood flow (Deutinger *et al.*, 1989; Steer *et al.*, 1990; Bourne *et al.*, 1990); it is doubtful, however, that these techniques have sufficient sensitivity to provide the desired observations. In addition, the momentary nature of the observations and their distance from the vascular beds in question may render the data irrelevant in the detailed understanding of tubal vascular function.

Blood flow in the larger blood vessels does not necessarily indicate the haemodynamics of the capillaries, the exchange vessels (Zweifach, 1977). Oviduct blood flow studies, in future, should be directed at an understanding of subepithelial capillary blood flow and hydraulic conductivity (or coefficient of filtration). It is relevant to know if the subepithelial capillaries are absorbing or filtering out electrolytes, fluid, protein, etc.; the net fluid flux, when documented, will enhance knowledge of the pathways used by ova/embryo derived factors to communicate, probably by cascade initiation (Yi-Qian Yang *et al.*, this volume), appropriate "messages" influencing tubal, ovarian and uterine function.

CONCLUSION

The many observations relating to human and rabbit oviduct vasculature reported in this paper suggest the complex role of the tubal vasculature and micro-vasculature in normal mammalian oviduct function. This is hardly surprising given the biological importante of normal tubal function in the preservation and maintenance of mammalian species. Tubal vasculature at its simplest, supplies "nutrients" and removes "waste"; at increasing levels of complexity the microvasculature may play an important role in gamete and embryo transport and, furthermore, provide a mechanism for biochemical communication between the oviduct, ovary and uterus.

The proposition that tubal MVA may contribute to gamete and embryo transport by circum-isthmic vascular occlusion, isthmic transudation and ampullary absorption requires examination in other species. In addition, it is necessary to determine the leakiness of tubal epithelial intercellular (gap) junctions. The freeze facture technique used by Murphy *et al.* (1981) is a suitable method for obtaining such observations. As it is likely that gap junction leakiness is focal in relation to intratubal ova or embryo(s), careful tissue preparation will be necessary.

Such data will stimulate the desire to further document the direction of tubo-ovarian venous drainage and the counter-current exchange of steroids, peptides and early pregnancy markers from the tubo-ovarian and uterine veins to the ovarian or uterine arteries. It is possible that the direction of tubal venous drainage changes from the ovarian vein, with counter current exchange to ovarian artery and thence "marker" transport to tube and ovary, to the uterine vein with counter current exchange to the uterine artery and thereby "communication" from the ovary and tube to the uterine vein thence to the uterine

artery and uterus. As suggested earlier in the text this counter-current exchange, depending on the venous connections may, in part, contribute to ones understanding of the pathophysiology of mild endometriosis.

The complex MVA of the rabbit oviduct, if observed in humans, could also contribute to our understanding of the pathogenesis of tubal ectopic implantation. A transient increase in vascular pressure or a transient reduction in venous wall tone may occlude the tubal lumen thus trapping an early embryo. When the clinical problem arises these transient changes would have resolved and, with the exception of the ectopic pregnancy, the tube is essentially normal (the common clinical experience).

There is, therefore, considerable opportunity for speculation on the precise role of the tubal vasculature, microvasculature and blood flow in oviduct function. Definitive experiments are, clearly, possible but will be technically difficult; the rewards, however, will be a substantial increase in our understanding of the complex interactions resulting in normal tubal function.

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