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EDITORIAL

OVARIAN LYMPHATICS— A POSSIBLE ROLE IN REPRODUCTION

The studies of Otsuki and Ichikawa and their respective colleagues in this issue describe the development of the lymphatic vasculature in the rabbit and rat corpus luteum. The role of the lymphatic drainage of the ovary as it relates to reproductive physiology is poorly understood. There is obviously considerable species variability (1,2). Consequently, the application of observations between species to the physiologic role of the lymphatic system is tenuous. Studies in rodents may not be applicable to larger animals, and considerable differences may be found between monovular species such as humans and polyovular species such as swine, rabbits, and rats. This is made clear by the occasional dire consequence of artificially induced multiple ovulation in women which results in hyperstimulation syndrome (3).

The ovary is an extremely dynamic organ. Hormonally its function varies depending on the time in the ovulatory cycle, producing predominantly estrogen in the follicular phase and progesterone in the luteal phase. In monovular species the non-ovulating ovary is relatively quiescent throughout the cycle. In the follicular phase the granulosa cells of the follicle are separated from the surrounding vasculature by a basement membrane. Androgens synthesized by the theca cells are believed to be the primary substrate for estradiol synthesis by the granulosa cells (4). After ovulation the basement membrane is penetrated and the corpus luteum is vascularized. Low-density lipoprotein cholesterol is now made available in quantities sufficient for the progesterone production associated with the luteal phase of the cycle.

The rapid growth of the ovulatory follicle and maintenance of the corpus luteum result in very high rates of blood flow to the active ovary. Baird and Fraser (5) estimated the blood flow to the very active ovary in women to be 2.6ml/gm/min. Niswender et al (6), using a sheep model, demonstrated that the blood flow to the ovary containing the corpus luteum was four- to six- fold that of the blood flow to the noncorpus luteum bearing ovary. In addition, using radioactive microsphere technique, they showed that the bulk of this increase in flow was directly to the corpus luteum rather than to the surrounding ovary. As the corpus luteum began to regress, anterio-venous shunts developed in the sheep corpus luteum. The concomitant development of a lymphatic system on the periphery of the corpus luteum or penetrating it with the newly developing vasculature seems a necessary, concomitant change. The dilatation of the lymphatics at the time of ovulation in the rabbit (7) and their persistent dilatation in the luteal phase is described by Otsuki et al. They further demonstrate the passage of what is probably transudate between the lymphatic endothelial cells. The physiologic importance of the lymphatics was shown by Linder et al (8) who demonstrated a rate of lymph flow of 100 to 600ml/hr/100gm of tissue from sheep ovaries which contained a corpus luteum. This rate of flow was greater than in any other organ studied in the sheep on a

per weight basis.

In the human, the capillary network associated with the development of the corpus luteum has not been so well described. However, it is probably not adequate to handle the increased amount of fluid which escapes from the ovarian vasculature. Maathus et al (9) have shown that there is a gradual increase in the peritoneal fluid volume in women during the follicular phase of the cycle from 1 to 7ml. In the early secretory phase this rises abruptly to approximately 20ml and remains near this level until the late secretory phase when it again diminishes abruptly. The latter is undoubtedly associated with regression of the corpus luteum. This fluid is a transudate which contains estradiol and progesterone concentrations during the luteal phase which are significantly above plasma concentrations. This transudate, with its increased levels of sex steroids, is believed to arise from the active ovary, as the peritoneal fluid volume in women on oral contraceptives which inhibit ovulation was less than 1ml.

The ovary contains numerous hormones in addition to steroids. Some, such as inhibin and oocyte maturation inhibiting factor, have known roles in regulating ovarian function. Others, such as vasopressin and oxytocin, have physiologic effects on the reproductive tract, but why they are present in ovarian tissue is not known. Oxytocin appears to be increased in the corpus luteum (10). Still others, such as prorenin (11) do not have clearly defined, specific effects on reproductive tissues. It is interesting to speculate on the possible role of lymphatics in transporting these hormones to other sites in the pelvis such as the Fallopian tube or uterus where they may have important functions in affecting motility or regional blood flow. In addition to showing very high levels of lymphatic flow from the sheep ovary, Linder et al (8) demonstrated progesterone levels in lymph which were as much as twice that of ovarian vein blood. The transudation of these hormones and of sex steroids into the peritoneal cavity may provide an important non-hematogenous route for delivery of high local hormone concentrations to target tissues.

The works of Otsuki and Ichikawa are thus a beginning. They serve as a stimulus, providing a morphologic background against which subsequent studies will hopefully develop to define the physiologic role of the ovarian lymphatic system.

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