

## **OVARIAN TRANSPLANTATION: NOW A REALITY?**

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Ovarian transplantation relies on the principle that the primordial follicles are more resistant to the side-effects of cryopreservation process. They are resistant because they are metabolically less active, their oocytes don't have a spindle like the metaphase II eggs, they are much smaller than prophase I oocytes, and they don't possess a zona pellucida like the later stage follicles. They are also the most abundant. Therefore, especially in the younger women, even a 50% loss due to the freezing process will still leave a significant number of follicles intact for a transplant. Studies in the rodent laid the foundation for the basic notion of ovarian transplantation, which was strengthened by the studies in the sheep. Finally, xenograft studies where human ovarian tissue was grafted under the kidney capsules of immunodeficient mice showed that in human ovary too, primordial follicles are most likely to survive and result in ovarian function. Based on these past data, we have initiated a human ovarian transplantation project. In the first phase, ovarian tissue was used only if it was removed for a benign ovarian condition. In the 32 year-old first patient, ovarian tissue was grafted in the forearm subcutaneously, akin to the method used for parathyroid gland transplantation. Tissue was also grafted in the broad ligament, adjacent to the uterine artery. Ultrasound follow-up 4 months after the procedures indicated that grafts were still intact, and some early antral follicle development was noted in the forearm by high-frequency ultrasound probes. A gradient was detected for estradiol, between the antecubital vein (which the graft drains to) and wrist vein, indicating hormonal production by the graft. In the second patient, frozen-banked tissue was thawed 8 months after storage, sawn together microscopically to form 2 large grafts, and transplanted laparoscopically in the ovarian fossa. Four months after the procedure, the 29 year-old patient was stimulated with menopausal gonadotropins. A dominant follicle reached 17 mm in maximum diameter and E2 peaked at 94 pg/mL. After hCG injection, the follicle collapsed and progesterone levels peaked at 13 ng/mL. In addition, testosterone levels showed a significant increase from the peritransplant levels of  $15.6 \pm 21$  to posttransplant levels of  $38.3 \pm 3$  ng/dL ( $P=0.0002$ ). Patient had menses 14 days after the first hCG injection. Her day 3 FSH and E2 on her first spontaneous menses were 17 pg/mL and 16 mIU/mL. In conclusion, these first cases of orthotopic and heterotopic ovarian transplants pave the way for further studies to establish this procedure as a clinically useful one.