

The Infertility Center of St. Louis

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Fresh and Cryopreserved Ovary Transplantation And Resting Follicle Recruitment

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Background

Ovary freezing and transplantation has garnered increasing interest as a possible way to preserve fertility for cancer patients and even for the decline in fertility, which naturally occurs in all women with aging. Yet these are mostly case reports with no consistent "denominator" to indicate success rates, and no scientific analysis of the mechanism of resting follicle recruitment, no insight on ovarian function in humans, that should be obtained from the analysis of results with ovarian transplantation. That is the purpose of this report.

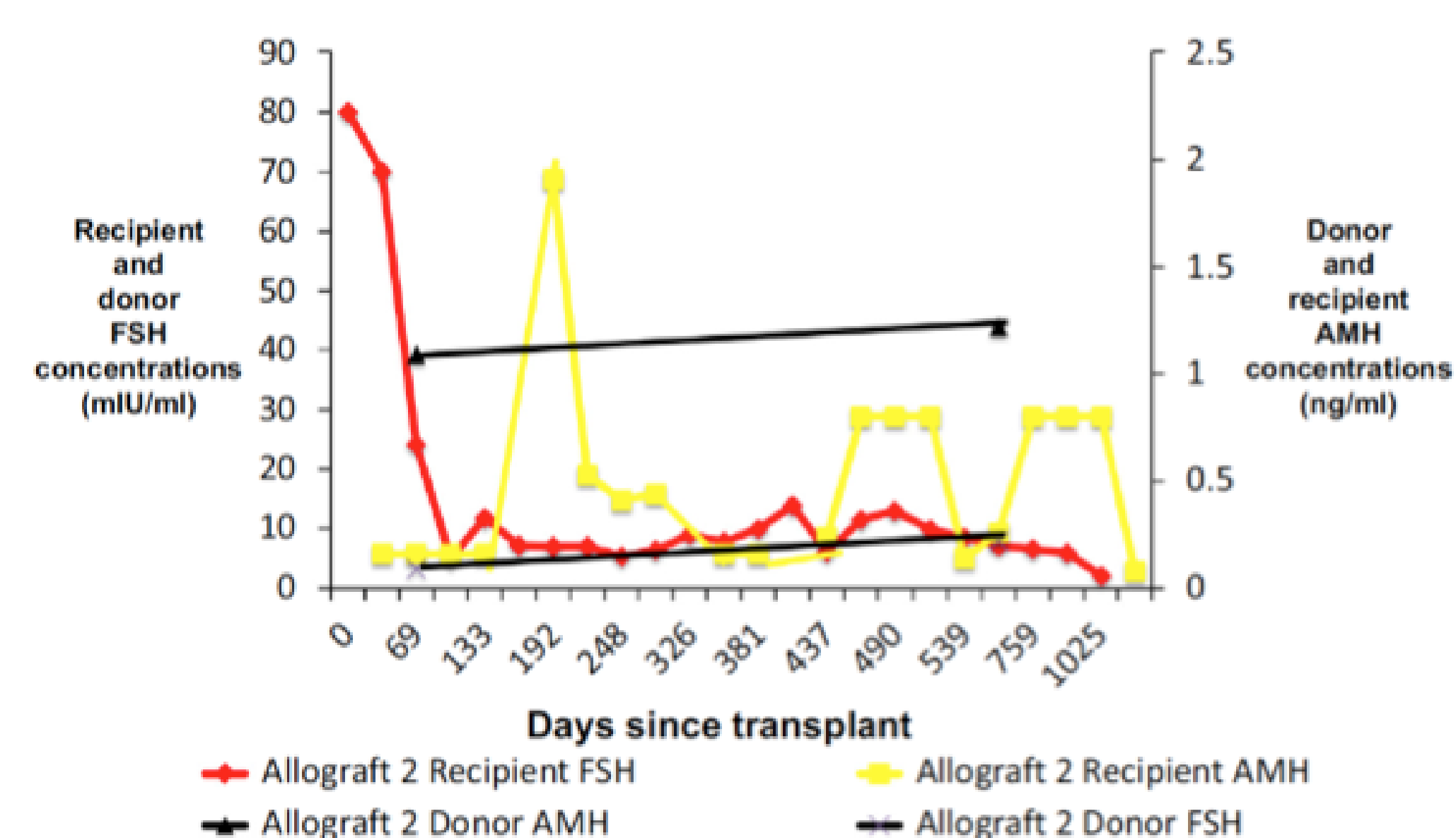
Method

Twenty-two women underwent fresh donor ovary or frozen ovarian cortex transplantation in one center with one surgical technique over a decade of follow up. Eleven were fresh and eleven were frozen. Recovery in recipients was measured by return of menses, day 3 FSH, LH, estradiol, AMH, ultrasound, pregnancy and delivery of a live baby.

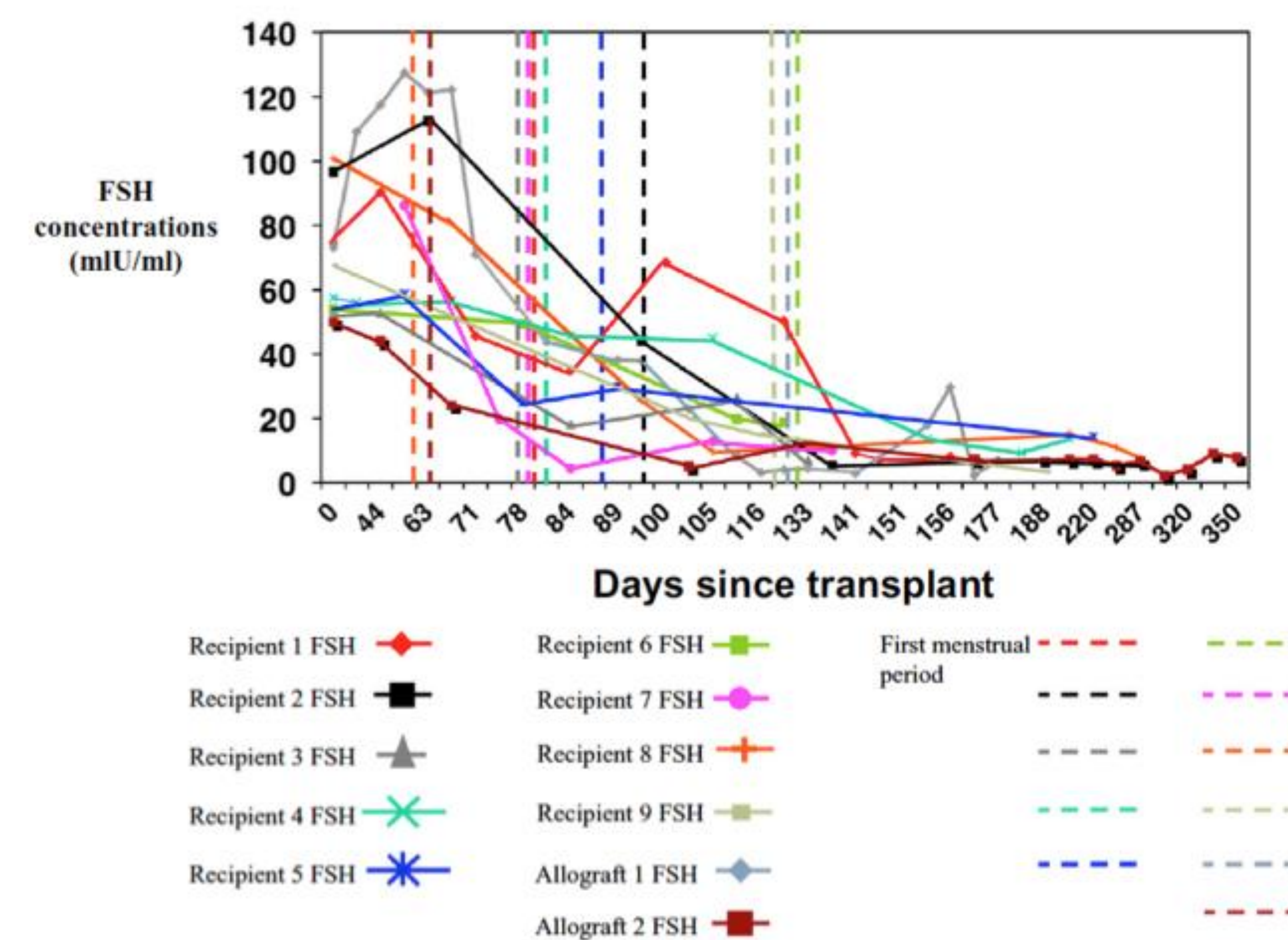
Results

All recipients of fresh or frozen ovarian transplants had the same robust return of normal FSH by 150 days, menstruation by 130 days, and massive AMH elevation by 170 days. The AMH then fell to below normal by 240 days and remained at that level for many years with normal ovarian cycling and hormonal function. 19 babies resulted from 11 fresh and 11 frozen cycles. Grafts of 1/3 of an ovary cortex lasted as long as 8 years or more. There was no difference between results with fresh or with frozen ovary. 75% had a successful pregnancy as a result.

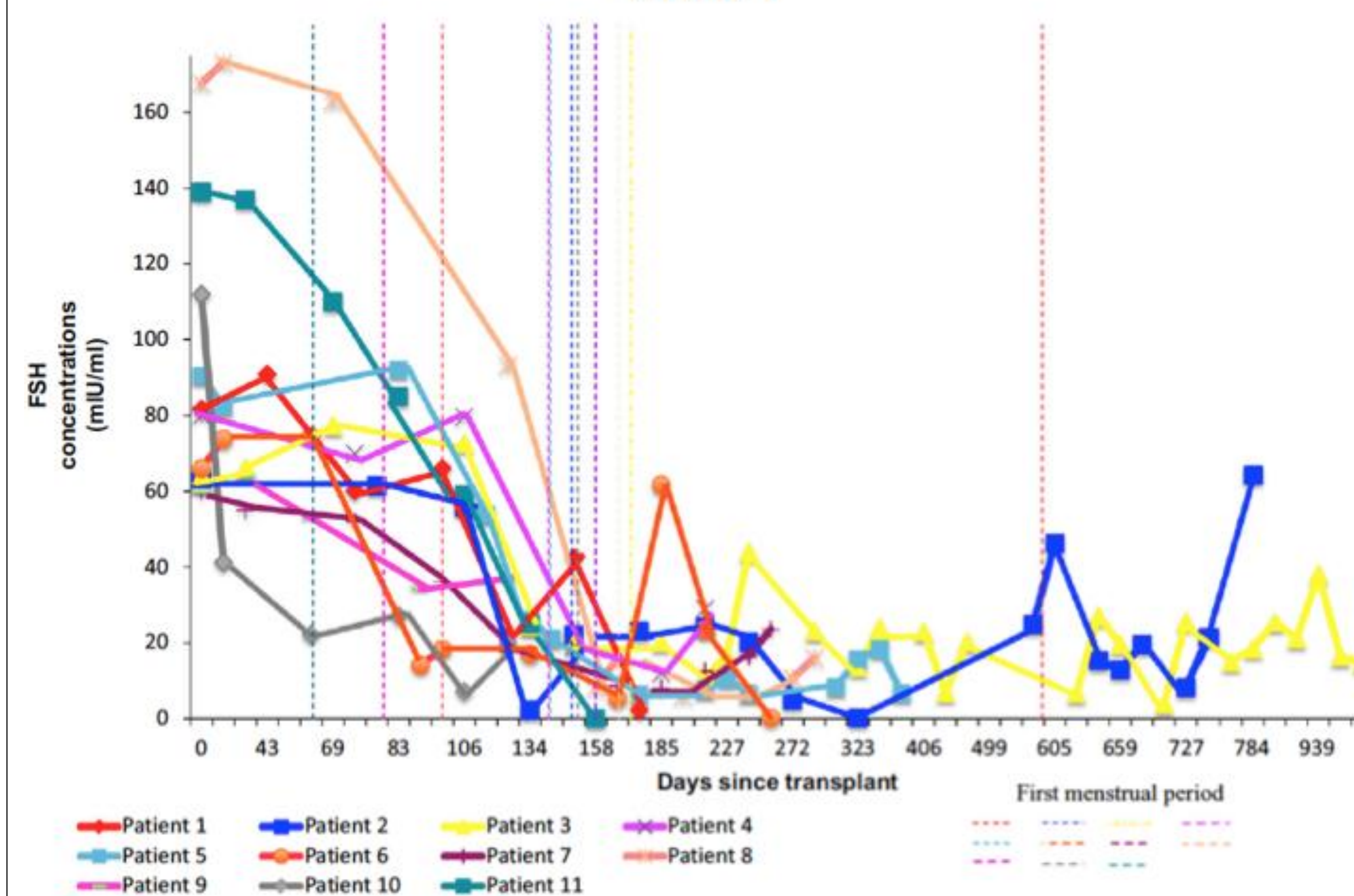
Levels of FSH and anti-Müllerian hormone levels in donor and recipient



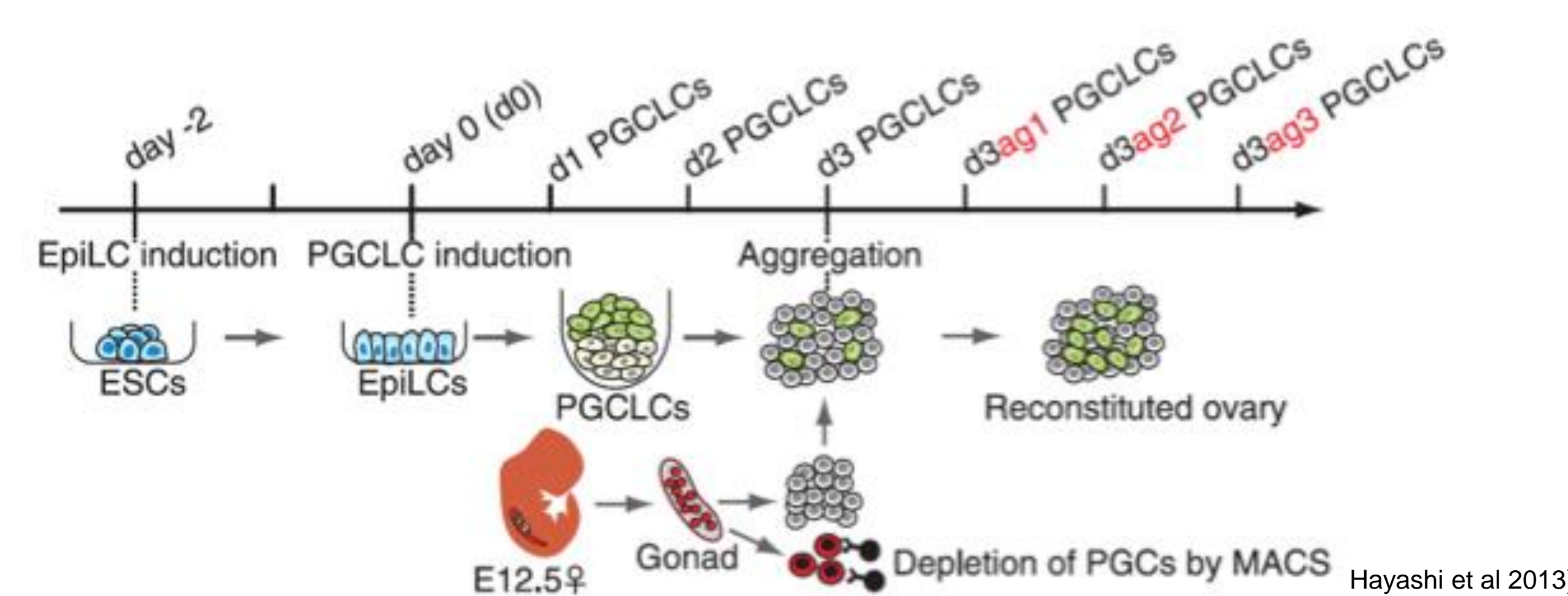
Recovery of Ovarian Function: Fresh



RETURN OF FSH TO NORMAL AFTER FROZEN OVARY GRAFT



Reaggregation of PGCLCs with gonadal somatic cells



Conclusion and Discussion

Ovary freezing and transplantation is clinically a robust method of preserving ovarian function, and it supports a number of basic concepts regarding ovarian primordial follicle dynamics. It seems to require about 4-5 months for primordial follicles to leave the resting phase and reach the ovulatory stage. In addition, after either fresh or frozen transplant, there is a brisk over-recruitment of resting follicles apparent by a massive increase in AMH at about 140 days, followed by a severe decline at about 240 days.

We suggest a unifying hypothesis that ovarian stromal density gradient can account for the early meiotic arrest of fetal oogonia, and also for primordial follicle recruitment in the adult. The mechanism of primordial follicle arrest and recruitment is the whole key to understanding ovarian function, ovarian reserve, and oogenesis.

In vitro IPS cell culture to mature oocyte in the mouse reveals that the primordial follicle is the main obstacle to in vitro oogenesis. When PGC like cells are aggregated with granulosa cells, the development of gonadotropin sensitive secondary follicles is "automatic". However with ovarian tissue culture (as opposed to IPS and PGC cell culture) the primordial follicles of ovarian tissue are "locked", which is their function, in order to prevent a simultaneous recruitment and subsequent loss of all the oocytes.

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