

Background

The endometrium is a complex tissue that has the capacity to undergo changes in response to steroid hormones, with the purpose of creating a receptive state with the arrival of an implanting blastocyst (Figure 1). Unfortunately, some women have repetitive implantation failure (RIF) that may be related to a lack of synchrony between the embryo and the endometrium. Endometrial Receptivity Analysis (ERA) testing (Figure 2) has shown that approximately 25% of women with RIF had non-receptive endometrium when tested on the expected day of implantation (1). Subsequent ERA testing to identify the patient's receptive window of implantation may improve implantation and pregnancy rates with embryo transfers

Objective

To determine if ERA testing will improve implantation and pregnancy rates in patients undergoing hormone treated frozen embryo transfer (HT-FET) cycles.

Materials and Methods

We performed a retrospective study of all patients who had one or more ERA tests (Igenomix) in our clinic from 2014 to 2017. Patients were treated with oral and/or vaginal estradiol and begun on vaginal or intramuscular progesterone when the endometrial thickness was 7 mm or more and the serum progesterone level was less than 1.5 ng/ml. The first endometrial biopsy ERA test was done on the sixth day of progesterone (P + 5). Patients who had a receptive ERA on day 6 of progesterone had a HT-FET with the transfer on day 6 of progesterone. Patients who had a pre-receptive ERA on the sixth day of progesterone were offered a repeat ERA day 7 of progesterone (P + 6). Patients with a receptive ERA P + 6 had a subsequent HT-FET on P + 6. A serum quantitative hCG was drawn 9 days after a blastocyst HT-FET and repeated 48 to 72 hours later. A transvaginal ultrasound was performed by 7.5 weeks estimated gestational age. Statistical calculations were performed with a Chi-Squared test.

Figure 1. Changes in sex hormones and the endometrial lining during an ovulatory menstrual cycle

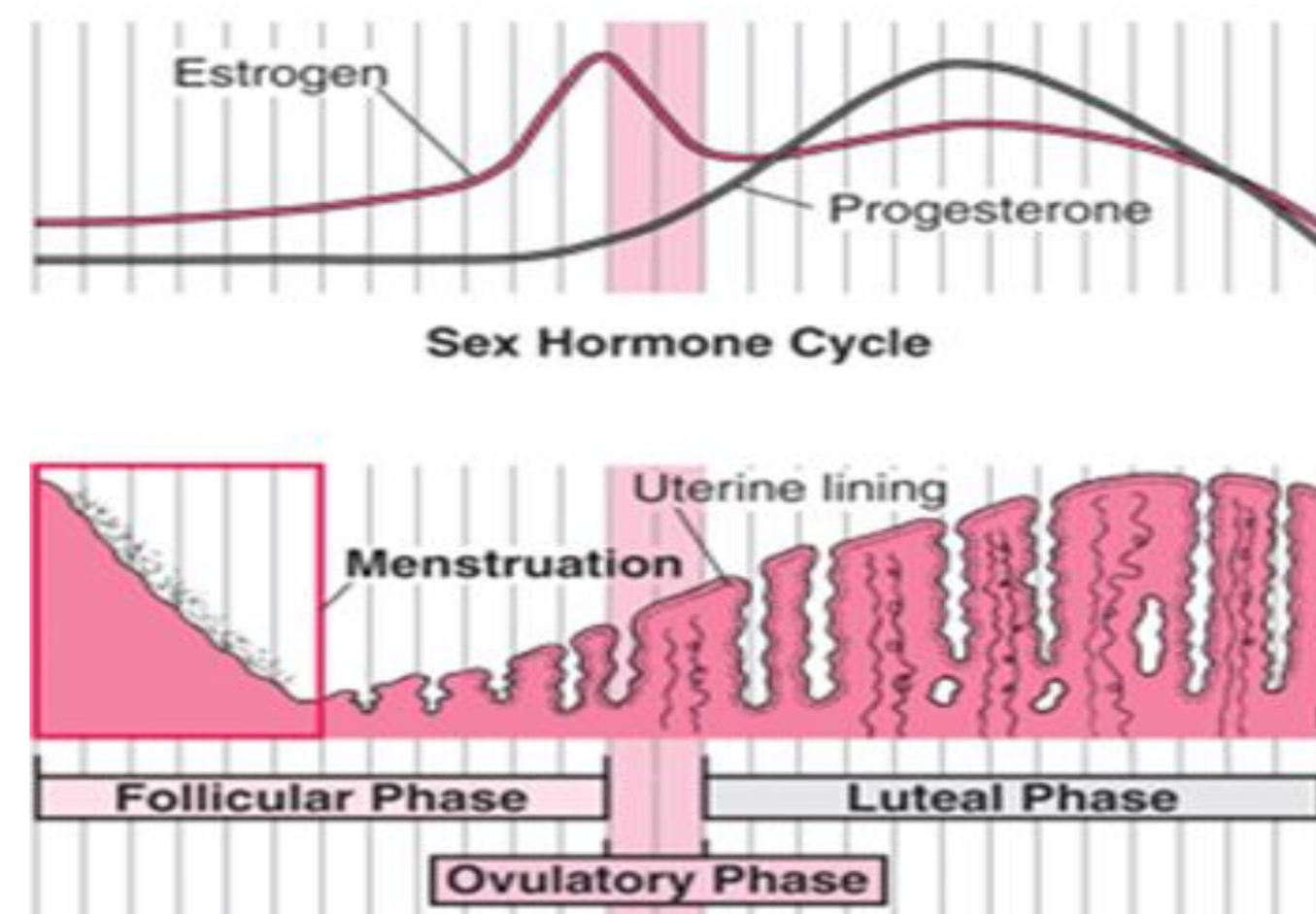


Table 1. ERA Receptivity results on day 6 of progesterone (P+5) or day 7 of progesterone (P+6).

	P + 5 (n=187)	P + 6 (n=67)	p
Receptive (%)	39.0	76.1	0.01
Pre-Receptive (%)	58.2	7.4	0.01
Post-Receptive (%)	2.8	16.4	0.01

Figure 2 . Endometrial Receptivity Analysis uses Next Generation Sequencing Technology to analyze expression levels in 236 genes involved in endometrial receptivity. A computational predictor analyzes the data and classifies the endometrium in the window of implantation (WOI) as pre-receptive, receptive, or post-receptive.

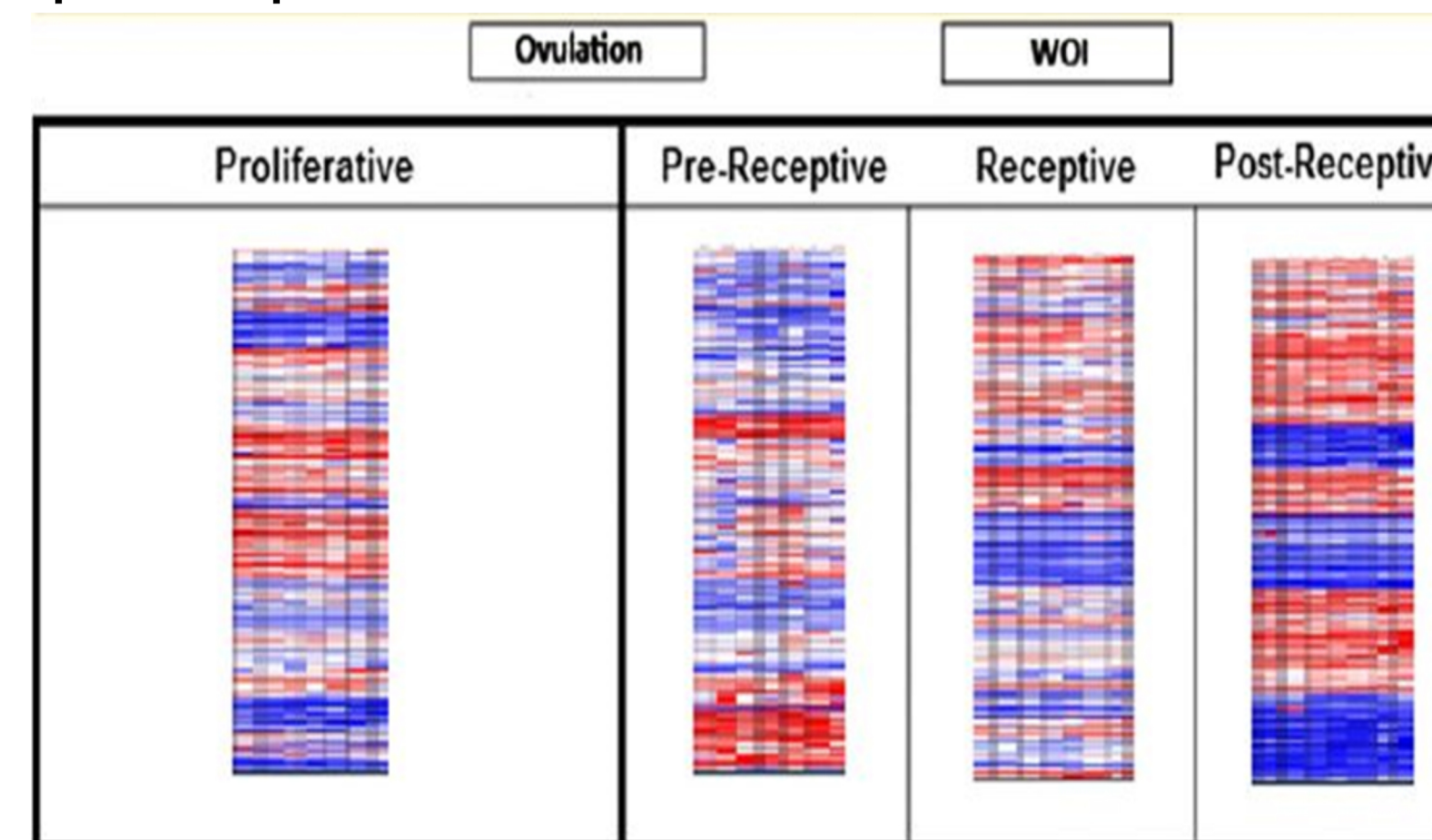


Table 2. Pregnancy and Ongoing Pregnancy results for HT- FET with a receptive endometrium on P + 5 or P+ 6

	P + 5 (n=46)	P + 6 (n=43)	p
Positive hCG (%)	65.2	72.1	0.38
Ongoing Pregnancy (%)	52.2	51.7	0.89
PGS Euploid Embryo (%)	67.3	65.9	0.88
Patients with Previous Unsuccessful FET (%)	60.9	78.0	0.71
Double embryo transfer (%)	10.8	14.6	0.59

Results

A total of 187 women, 27 to 51 years of age had an ERA test on the sixth day of progesterone treatment (P + 5). Only 39% of the ERA tests on P + 5 were receptive. Repeat ERA testing on day 7 of progesterone (P + 6) was performed on 67 women. The majority of P + 6 ERA tests were receptive (76%). Eighty eight percent of patients had a single embryo transfer and twelve percent a double embryo transfer. The positive hCG and ongoing rates were similar in women having an HT-FET on P + 6 or P + 7 when there was an ERA confirmed receptive endometrium.

Conclusions

Women undergoing an ERA test were significantly more likely to have a receptive endometrium on the seventh day of progesterone (P+6), compared to the sixth day of progesterone (P+5). The non-receptive ERA results for our clinic were much higher than reported in the initial study (2). There were excellent ongoing pregnancy rates with HT- FET when there was a confirmed receptive ERA.

References

1. Diaz-Gimeno P, Ruiz-Alonso M, Belsa D, et al. The accuracy and reproducibility of the endometrial receptivity array is superior to histology as a diagnostic method for endometrial receptivity. Fertil Steril 2013;99:508-17.
2. Ruiz-Alonso M, Bleaa D, Diaz-Gimeno P, et al. The endometrial receptivity array for diagnosis and personalized embryo transfer as a treatment for patients with repeated implantation failure. Fertil Steril 2013;100:818-24.