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ENDOMETRIAL RECEPTIVITY ANALYSIS

Introduction :

Human implantation is a complex process requiring synchrony between a healthy embryo and a functionally competent or receptive endometrium

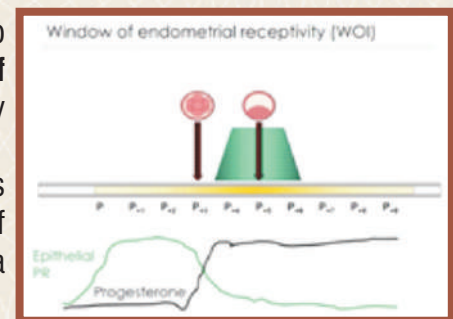
The bottleneck for IVF ICSI program is Implantation. Because in an ivf/icsi cycle we have made sure that the fertilization takes place (unlike in an IUI or in a natural attempt at home) and have used the assistance of USG to monitor the right time for embryo transfer according to the endometrial pattern.

Endometrial Receptivity (ER) is an important parameter for successful implantation, especially in IVF treatment where, in each cycle, embryo transfer is to be performed at a specific time.

Advent of "Omics" that is, the analysis of biological samples using molecular profiling has revived interest in the study of Endometrial Receptivity particularly in the context of implantation failure (IF) in IVF. After many years of research, decoding endometrial transcriptomics using next-generation sequencing (NGS) and thus identifying the personalised window of implantation (pWOI) is now possible¹

What is Endometrial Receptivity ?

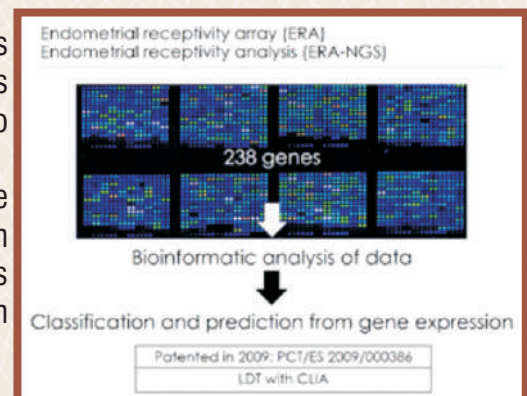
The endometrium is receptive when it is ready for embryo implantation to occur. This period of receptivity is called the **window of implantation(WOI)**. The WOI is defined as the window of opportunity during which the endometrium becomes maximum receptive to embryo. Each woman has a unique window. For some women the window is shorter and/or displaced. By knowing your personal window of implantation, you can optimise your chances of pregnancy through a personalised embryo transfer.



What is Endometrial Receptivity ?

ERA is a customized test to analyse 238 genes expressed at various stages of the endometrial cycle in a given sample. It evaluates endometrial receptivity to determine the optimal time for embryo transfer and when the endometrium is ready for implantation.

By investigating the gene expression profile we can evaluate the endometrial receptivity or understand the window of implantation which is the clinical parameter for reproductive health. It evaluates 238 genes involved in endometrial receptivity and can tell us when the endometrium is ready for implantation.



Who needs it or indications?

- Recurrent Implantation failure patients :
 - 2 or more implantation failures with own embryos or 1 with ovum donation
 - Good euploid embryos
- Patients with morphologically normal endometrium :
 - ERA after intervention in the case of an congenital uterine anomalies
- Patients with normal, atrophic or hypertrophic endometrium
 - In case of atrophic or hypertrophic, it has to be consistent for all the cycles in the patient.

ERA PROCEDURE – Preparation and Biopsy

The test could be done in natural , modified natural cycle or hormone replacement therapy (HRT) protocol, according to the protocol to be used at time of frozen embryo transfer.

It just needs a standardized endometrial biopsy once the endometrium is prepared through the described protocols.

Natural Cycle :

EB in natural cycle done at Luteinising hormone (LH) + 7

- LH surge can be detected in urine or blood once the follicle is 15 mm on USG
- The day of LH surge is LH + 0 and the sample taken 7 days (168 hours) after that (LH + 7)

Modified Natural cycle (Natural cycle with hcg -hcg + 7)

- hCG will be routinely administered once the follicle size is 17 mm or more
- The day of hCG is hCG + 0, EB will taken on hCG + 7

HRT protocol (P + 5)

- The most preferred method due to its easy execution and lesser cancellations.
- Tablet estradiol valerate 6-8 mg is started from day2/3 of menses and continue till the TVS scan reveals the desired endometrial thickness (6mm or more trilaminar pattern) , normally its around 10 days .
- Once the endometrium is ready send the progesterone test to rule out any ovulation and start the progesterone in same dose and formulation as it will be at time of embryo transfer and to do the EB post 5 days of progesterone in case of blastocyst transfer or at 120 hours

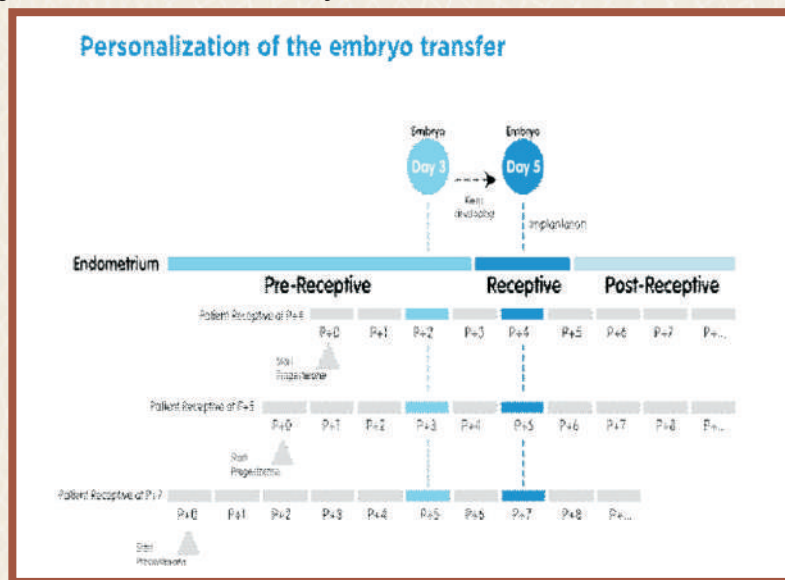


Fig 1 : Personalised embryo transfer recommendation based on endometrial receptivity analysis (ERA) results in HRT protocol¹

Please note ERA test cannot be done in a stimulated cycle.

STORAGE

- Keep in fridge (4 – 8c) for 4 hrs.
- This preserved sample, in cryotube can be immediately shipped at room temp.
- Sample at room temp should reach the main lab within 4 to 5 days.
- Results will be ready in 20 days after receiving samples.

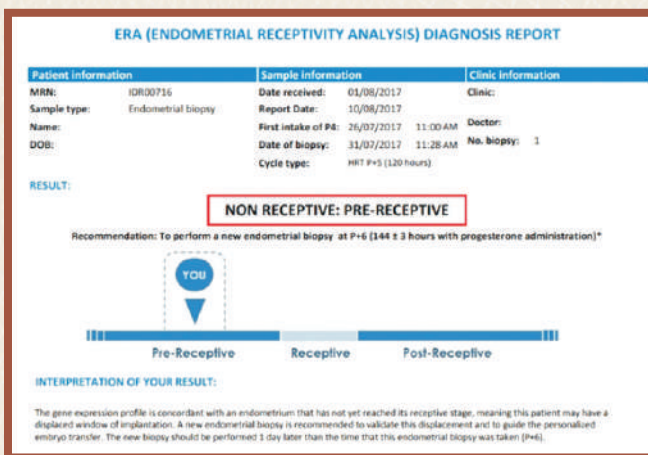
Interpretation of results

- Receptive – Suggests that the gene expression profile is similar to that of a normal receptive endometrium. The ET will be performed under the same conditions and timing in which the biopsy was taken
- Non-Receptive – Suggests that the gene expression profile is not similar to that of an endometrium of receptive phase.
 - Pre-Receptive- The endometrium has not yet reached the optimal stage of receptivity
 - Post-Receptive - The optimal stage of receptivity has passed

With the above results a recommendation is also given for the timing of WOI for the personalized embryo transfer (pET). In some cases, to validate this pWOI, a second biopsy may be recommended as per the time recommendation given.

A receptive result indicates the ideal day of blastocyst transfer. If the embryo is of day 3, it should be transferred 2 days earlier than the recommended ERA result.

This is how the results would look like



Non-receptive -Pre-receptive result



Non-receptive- Post-receptive

Conclusion :

ERA test is very sensitive in identifying the genetic expressions of the endometrium to tell us the exact embryo transfer time. pET or personalised embryo transfer can help to increase the success rates (PR and IR) significantly. It is of vital help especially in cases of recurrent implantation failures where we are clueless about the reason behind the negative ivf result.

References

1. Igenomix (2009) .ERA Endometrial Receptivity Analysis (Online) Available from <http://www.igenomix.com>
2. Diaz -Gimeno P, Horcadjadas JA, Martinez-Conejaro JA, et al. A genomic diagnostic tool for human endometrial receptivity based on transcriptomic signature. Fertil Steril 2011;95:50-60
Compared to other methods, the accuracy of ERA test is much better (sensitivity of 0.997 and a specificity of 0.885)²