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Frozen And Fresh Embryo Transfer Implantation On Endometrial Preparation : A Comprehensive Review

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Abstract: *Endometrial Preparation plays a pivotal role in the success of in vitro fertilization (IVF) procedures. This paper provides a comprehensive review of the assessment of endometrial Preparation in FET cycles, focusing on the emerging role of Fresh and frozen embryo transfer (ET) are pivotal techniques in ART, each with distinct implications for endometrial preparation and pregnancy outcomes. This abstract delves into the intricate interplay between embryo transfer methods and endometrial receptivity, shedding light on their impact on successful implantation and live birth rates.*

Key words: *IVF In vitro fertilization, FET Frozen embryo transfer , ET Fresh embryo transfer, assisted reproductive technology (ART)*

Introduction :

1.1 INFERTILITY.

Infertility is thought to affect approximately 15% couples of reproductive ages worldwide. Infertility is therefore defined as a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 or more of regular unprotected sexual intercourse (WHO, 2021).

It may occur due to male factors, female factors, or may be unexplained.

1.2 Overall The fertility rate (TFR)

In India from 1950 - 2023 was 2.1 births per woman. the WHO estimates the prevalence of infertility in India to be between 3.9% and 16.8%.There are many reason for infertility, including some that can be treated with medical involvement or some may not be resolved / unexplained. Primary infertility is the inability to have any pregnancy, while secondary infertility is the inability to have a pregnancy after previously successful conception, Infertility may occur due to male factors, female factors, a combination of male and female factors or may be unexplained. For both women and men, however, lifestyle factors such as smoking, excessive alcohol intake and obesity have been associated with higher chances of infertility.

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The rates of primary infertility, as reported by women, ranged from 1.5% to 2.6%, which were much lower than those reported over the course of 12 or more months. The male contribution to these rates of infertility ranged from 0.4% to 1.82% according to WHO estimates.

The rates of secondary infertility is (5.8%)

The rate of unexplained 15-30%

The rate of infertility in both male and female is 25-40% due to complications in both cases.

1.3 FEMALE INFERTILITY

Around 35% couples will have infertility of primarily female origin. The causes include ovulatory dysfunction, fallopian, uterine or pelvic abnormalities including endometriosis, & advanced maternal age.

Female fertility is a complex multi factorial and polygenic disease associated with genetic

factors which play essential roles in the formation and development of follicle and oocyte

maturation.

Women with health problems such as obesity and diabetes often increase their risk of childbirth. More than 40% of women who go to infertility clinics are found to be overweight. Infection, fibroids and genital TB ,'PCOS' Polycystic ovarian syndrome, Endometriosis, Edometrial polyps, Uterine myoma, Adenomyosis,Edometrial hyperplasia ,Edometrial hypertrophy ,Edometrial cancer ,Endometrial neoplasia or adenocarcinoma this are some factors may lead to infertility in female.

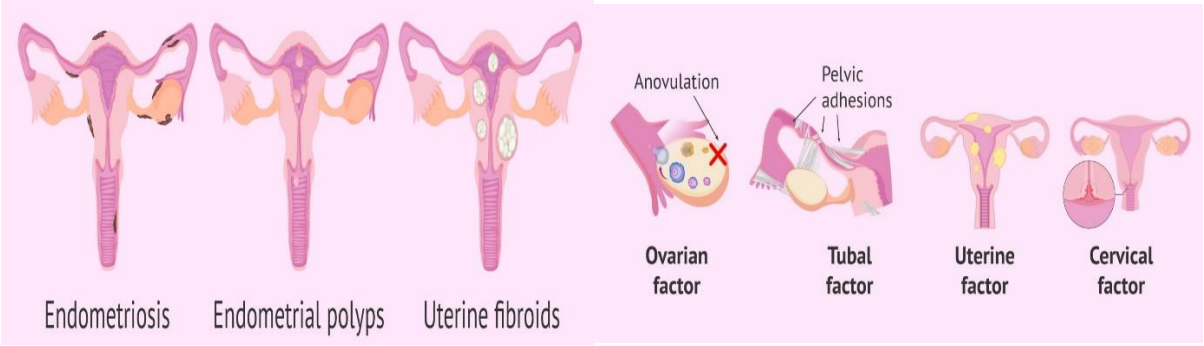

Fig 1 : Female Reproductive disorders

Adapted From :https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fendometrium%2F&psig=AOvVaw0gSKfouPctXZHXI-ILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABAE.

https://www.invitra.com/en/wp-content/uploads/2018/09/causes-of-female-infertility.png.

2.1 Definition of terms :

IVF: In vito fertilization and is a complex veries of procedures need to reproduce or prevent genetic problems and aid in conception. In vitro fertilization is the process of conception in which an egg is fertilized with a sperm outside the body, in vitro ("glas").This process involves monitoring and regenerating the women's reproductive process, removing the egg or eggs from the woman's ovary and allowing the sperm to fertilize them in the laboratory condition. After the fertilized egg (zygote) has passed the fetal culture for 2-6 days, it is implanted in the same or another woman's uterus, with the aim of establishing a successful pregnancy.

Ovaries: The ovaries are the female gonads. the main reproductive organs of women.These glands have three important functions: they release hormones, protect a woman's ovaries, and release her eggs during pregnancy. **Ovulation:** ovulation

is the release of an egg from your uterus, inserted into your fallopian tube. It occurs about 13-15 days before the start of each period. As with your period, the time of ovulation can vary from cycle to cycle, and you may have an irregular cycle where you do not stop at all. After maturation, during the luteal phase, the egg will be fertilized to fertilize the sperm. In addition, the lining of the uterus (endometrium) is strong enough to detect a fertilized egg. If no pregnancy occurs, the uterine lining and blood will be drained during menstruation.

Induced Ovulation: Ovulation implementation is a promising reproductive technology in

patients with conditions such as poly-cystic ovary syndrome (POS) and Oligo menorrhea. It is also used in in vitro pregnancy to make mature follicles before fertilizing eggs.

Unexplained infertility. Unexplained infertility means no cause of infertility has been found

despite evaluation for common causes.

3. Objective :

A Comprehensive Review on Frozen And Fresh Embryo Transfer Implantation On Endometrial Preparation

3.1The statement:

Why Endometrial Preparation plays a important role in Embryo Transfer

3.1.2The Null Hypothesis:

- The endometrial preparation and profile is one of the main variables to be evaluated in women undergoing an embryo transfer procedure using self or donor oocytes, and also in frozen-thawed embryo transfers. In order to carry out the embryo transfer, an endometrial preparation is needed.
- Optimization of endometrial preparation protocols before frozen embryo transfer is mandatory to further improve pregnancy outcomes.

4.1 RIVIEW LITERATURE :

Endometrial preparation or priming plays a main role in IVF treatments, especially with donor eggs or in Frozen Embryo Transfers (FETs), Fresh Embryo transfer .

- Endometrium is a innermost mucous layer that lines the uterus , it is a most important reproductive organ were gestation takes place for nine months .

Its function is to thicken during the menstrual cycles if fertilization doesn't takes place then the lining starts to shed off andits another function is to allow the embryo to implant .

- Myometrium is a thick middle muscle layer of the corpus or fundus . its main functions it expainds during pregnancy to hold the growing fetus.

It contracts during labor to push the baby out

- Perimetrium / Serous coat of uterus: it is a outer most layer of the uterus . its function is to maintain the structural integrity of the uterus by providing support and protection.

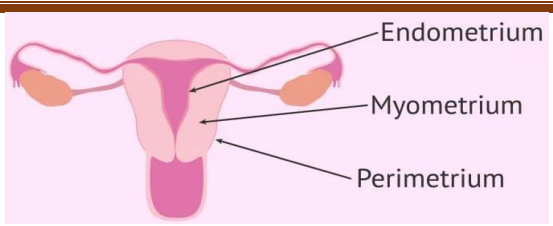

Fig 2: Uterus lining.

Adapted From https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fendometrium%2F&psig=AOvVaw0gSKfouPctXZHXI-ILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABAP

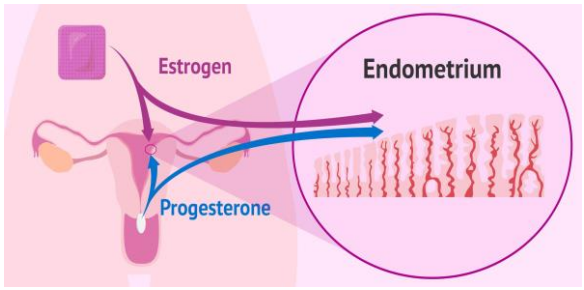

Fig 3 : Endometrium with blood flow.

Adapted Fromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fpreparation-of-the-endometrium%2F&psig=AOvVaw0gSKfouPctXZHXI-ILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABAX.

The spiral arteries supply blood to the endometrium of the uterus, more specifically, the functional zone (Endo lining) which sheds off during menstruation.

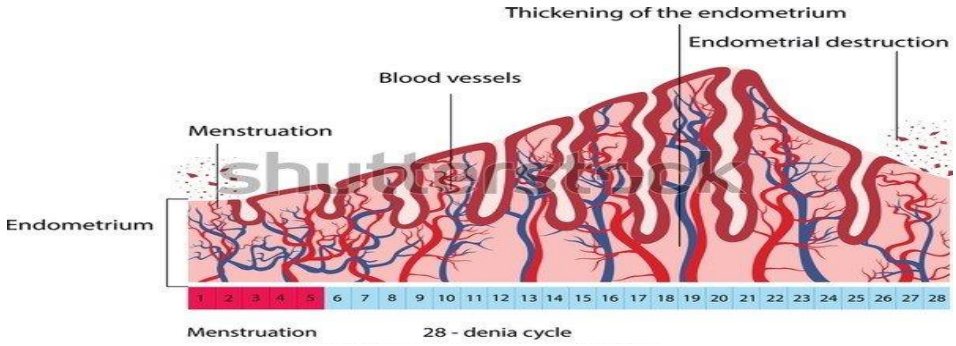

Fig 4: Blood vessels in endometrium.

Adapted Fromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.quora.com%2FDuring-which-stage-of-the-menstrual-cycle-does-the-endometrium-layer-thicken&psig=AOvVaw0gSKfouPctXZHXIILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABAn.

4.2 Implantation in the endometrium

Nesting of the embryo in the endometrium occurs when about 6 to 7 days have passed since fertilization and When the embryo is at the blastocyst stage.

For this to occur, there must be a perfect synchronization between the embryo and the endometrium, that is, there must be **endometrial receptivity**.

The endometrial receptive is known as ***implantation window***, which lasts approximately 4 days.

The ideal endometrial thickness for implantation is **7-10 mm**. Embryos typically cannot implant in an endometrium that is less than **6 mm** thick.

When the egg is fertilized and the embryo is implanted, the secretory endometrium becomes more specialized due to the effects of estrogens and progesterone, a process known as decidualization.

Decidualized endometrium consists of a specialized structure that will give rise to the placenta during gestation and will participate in the exchange of gases and nutrients between the mother and the embryo.

4.2.1 The following tests are useful for measuring endometrial thickness, as well as endometrial receptivity:

- Transvaginal ultrasound

With ultrasonography, it is possible to differentiate the following types of the endometrium:

- Type 0 endometrium
  During the menstrual phase, the endometrium is hyperechogenic, i.e., it is seen as a thin, faint white line <5 mm.
- Type I endometrium
  Presents a trilamellar pattern, that is, the appearance of three lines parallel to each other, although the inner line is not well distinguishable. It is observed in the proliferative phase.
- Type II endometrium
  The endometrium is clearly trilaminar, the three lines are perfectly distinguishable. The endometrium can measure between 7 and 10 mm. It is observed in the proliferative phase shortly before ovulation, due to the strong influence of estrogens.
- Type III endometrium
  It is seen in the luteal phase of the cycle, so the endometrium is in the secretory phase under the influence of progesterone, and is ecorefringent (homogeneous). The endometrium is thickened, has fluid content and glycoprotein material in the endometrial glands.

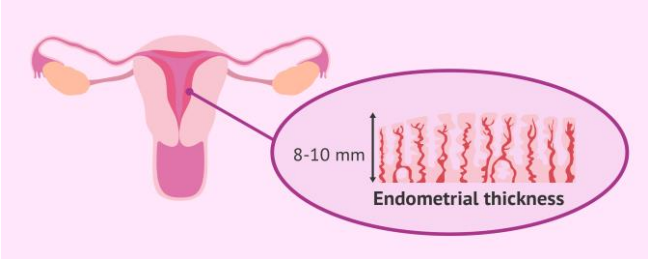

Fig 5 : Endometrium Thickness

Adapted Fromhttps://www.google.com/url?sa=i&url=http%3A%2F%2Fhotcore.info%2Fbabki%2Fendometrial-lining-thickness-after-menopause.htm&psig=AOvVaw0gSKfouPctXZHXIILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABBO.

4.2.2. Additional techniques

If transvaginal ultrasound is not sufficient to assess endometrial structure and thickness, or if further analysis is necessary in order to determine endometrial receptivity, the following techniques may be used:

- **Hysteroscopy**
  To assess endometrial quality and act on pathology, if present.

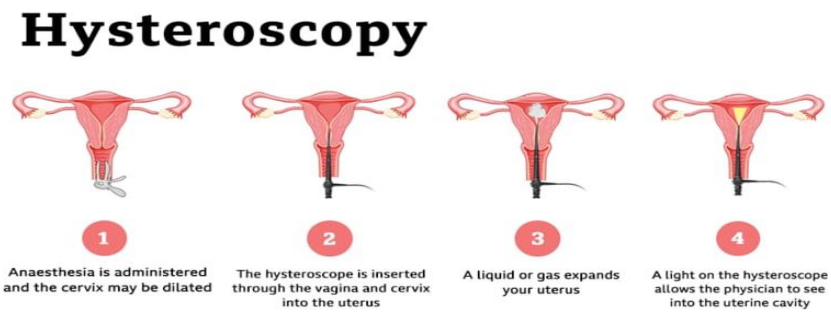

Fig 6 : Hysteroscopy

Adapted From https://ichef.bbci.co.uk/news/1024/cpsprodpb/F82C/production/_131823536_microsoftteams-image-150.png.webp

- **ERA (endometrial receptivity array)**

To detect the presence of genes involved in endometrial receptivity, which allows knowing if the endometrium is receptive at a particular time and if it is able to implant embryos.

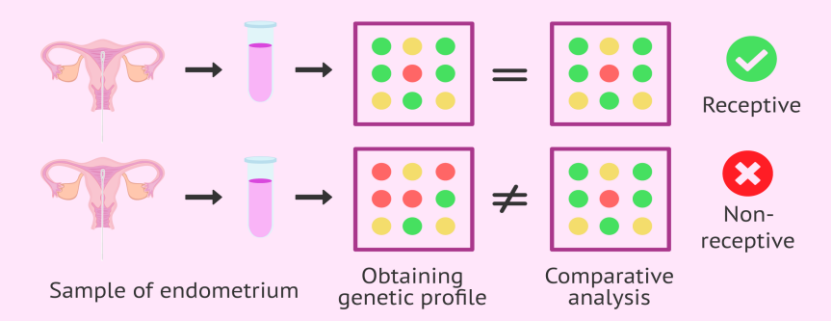

Fig 7 : ERA

Adapted From https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fendometrial-receptivity-test%2F&psig=AOvVaw3GwsrkUbA1d7i-__A1SIfd&ust=1717492385519000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCMCG_vCLv4YDFQAAAAAdAAAAABAJ.

- **PRP (Platelets Rich Plasmid)**

Platelet-rich plasma (PRP) therapy has been used in fertility treatments for women with very low ovarian reserve and premature ovarian insufficiency. Which helps in thickening of Endometrium.

Its main function in fertility treatment is to improve the endometrium receptivity it is done before 48 hrs of Embryo transfer .

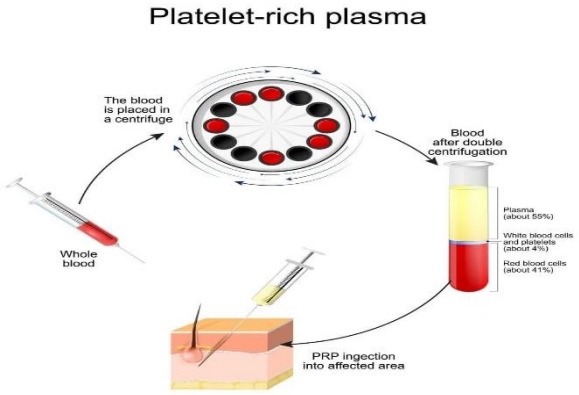

Fig 8 : PRP Therapy

Adapted From http://www.kochancenter.com/wp-content/uploads/2019/10/PRP_rev_illo_281209340-768x761.jpg.

3.1 FRESH EMBRYOTRANSFER

Fresh embryo transfer (FET) is a crucial component of assisted reproductive technology (ART), particularly in the context of in vitro fertilization (IVF).

In Fresh ET it involves the immediate transfer of embryos into the uterus during the same cycle of ovarian stimulation,

The process begins with ovarian stimulation, where fertility medications induce the ovaries to produce multiple eggs. These eggs are then retrieved and fertilized in the laboratory. The resulting embryos are monitored and cultured until they reach an

optimal stage for transfer, often at the blastocyst stage (around day 5). Fresh embryo transfer aims to place the highest quality embryos into the uterine cavity to achieve successful implantation and pregnancy.

3.1.1 The Fresh Embryo Transfer Protocol

1.Ovarian Stimulation:

- Medications: The woman takes fertility drugs to stimulate her ovaries to produce multiple eggs.
- Monitoring: Ultrasound and blood tests monitor the development of the ovarian follicles.

2.Oocyte Retrieval:

- Procedure: When the follicles reaches 18- 20 mm then the trigger injection is given.Oocyte retrieval is done between 34-36 hrs after the trigger injection, a minor surgical procedure called OPU (Ovum pick up) the oocytes are retrieved from the ovaries.
- Anesthesia: This is usually done under sedation or anesthesia.

3.Fertilization:

- Insemination: The retrieved eggs are combined with sperm in the laboratory to facilitate fertilization.
- ICSI: In most of the cases, intracytoplasmic sperm injection (ICSI) is used to inject a single sperm directly into an egg.

4.Embryo Culture:

- Development: The fertilized eggs (embryos) are cultured in the lab for 2 to 6 days.
- Monitoring: Embryos are monitored for growth and quality.

5.Embryo Transfer:

- Preparation: The best quality embryos are selected for transfer.
- Transfer: The embryos are placed into the uterus using a thin catheter. This is usually a painless procedure.
- The endo thickness must be >7mm.

6.Luteal Phase Support:

- Medications: After the transfer, the woman may receive progesterone to support the uterine lining and facilitate implantation.

7.Pregnancy Test:

- Confirmation: About 10-14 days after the transfer, a blood test (beta hCG) is done to confirm pregnancy.

NOTE: Were the progesterone is given from the day of OPU till day 5 or day 3.

Fig 9 : Fresh embryo transfer showing complete OPU to ET

Adapted Fromhttps://d2jx2rerrg6sh3.cloudfront.net/image-handler/ts/20170220055647/ri/680/picture/IVF%20process%20infographic%20-%20ectorPot%20_thumb.jpg.

Several factors contribute to the decision to opt for fresh embryo transfer. These include the patient's age, the number and quality of embryos, and the response to ovarian stimulation. Fresh transfers can be advantageous because they avoid the potential risks and uncertainties associated with freezing and thawing embryos. Additionally, the synchronization of the embryo development stage with the endometrial receptivity is believed to be beneficial for implantation.

However, fresh embryo transfer is not without challenges. The ovarian stimulation process can sometimes lead to ovarian hyperstimulation syndrome (OHSS), a potentially serious complication. Moreover**, The Endometrial Environment Immediately Following Stimulation May Not Always Be Optimal For Implantation, Potentially Reducing Success Rates In Some Cases.**

4.1 Frozen Embryo Transfer:

A frozen embryo transfer (FET) is a procedure used in assisted reproductive technology (ART) where an embryo that was previously created through in vitro fertilization (IVF) and then cryopreserved is thawed and transferred into a woman's uterus. According to the World Health Organization (WHO), **FET has become a well-established practice in ART, providing flexibility in the timing of transfers and potentially reducing the risk of ovarian hyperstimulation syndrome (OHSS) compared to fresh embryo transfers.**

The process involves the careful thawing of cryopreserved embryos, which are stored in Liquid nitrogen at -196°C. These embryos are then transferred into the uterus, where they may implant and develop into a pregnancy. One of the key benefits of FET is that it allows patients to avoid the physical and emotional strains associated with the ovarian stimulation required for fresh IVF cycles.

FET can be scheduled at a time that is optimal for the patient, improving the chances of successful implantation by ensuring the endometrium is well-prepared. This scheduling flexibility can lead to better pregnancy outcomes and can be particularly beneficial for women with specific health conditions or those who need to delay transfer .

4.2The Frozen Embryo Transfer Protocol

4.2.1Preparation and Planning:

The process begins with a consultation where the patient's medical history is reviewed, and a personalized FET plan is created.

4.2.2The typical FET process

A FET cycle will take approximately 6 to 8 weeks. A cycle typically begins with 2 to 4 weeks of daily birth control pills to suppress the normal ovarian cycle, as it would lead to ovulation. After the course of birth control, you will need a baseline assessment involving bloodwork and ultrasound. Depending on the test results, your physician may instruct you to begin estrogen (pills or patches), oral medication (such as Femara), or injections (such as FSH) to build the uterine lining.

After a designated period of time on the hormonal medication, you will return for bloodwork and a transvaginal ultrasound lining check. If the lining check demonstrates that your hormone levels are appropriate and your endometrial lining has thickened, your physician will likely instruct you to add daily injections or vaginal suppositories of progesterone to your medication regimen.

Estrogen and progesterone supplementation continue after the transfer. Typically, a blood pregnancy test is checked 10-15 days after the embryo transfer. If you are pregnant, then hormone supplementation will continue until 10 weeks. If you are not pregnant, then Clinician will provide instructions to discontinue supplements in order to preparation for another cycle of FET .

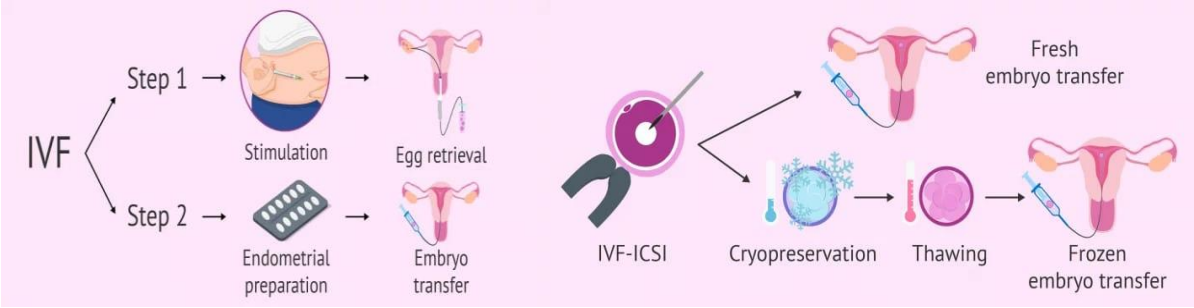

Fig 10 : FET process

Adapted Fromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Ffrozen-embryo-transfer%2Fivf-procedure-steps%2F&psig=AOvVaw2A_HXTHoN1FBA5dRxSzdDh&ust=1717493450777000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwjugcnpj7-GAxUWcmwGHXpwBnsQjRx6BAgAEBQ. https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Ffrozen-embryo-transfer%2F&psig=AOvVaw0TpR7aOj3hQbiUqMhvaQRQ&ust=1717493484085000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwjK_bn5j7-GAxWLfGwGHSS8BjQQjRx6BAgAEBQ.

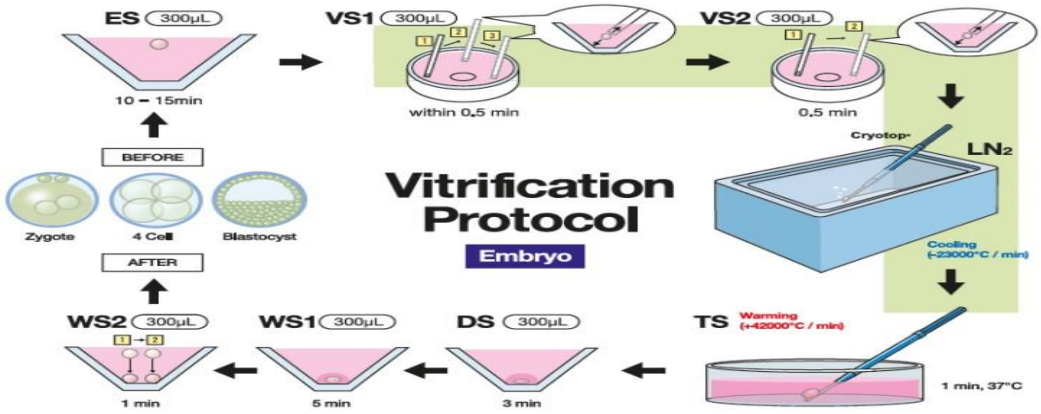

Fig 11: Vitrification Protocol

AdaptedFromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fkitazato-ivf.com%2Fachieve-higher-rates-with-a-globally-proven-protocol%2F&psig=AOvVaw1LmeRciVq8d7koGN_stmt-&ust=1717493382007000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwih0OPIj7-GAxUQTWwGHep1DQMQjRx6BAgAEBQ.

4.3Endometrial Preparation:

This can be done in a natural cycle, where the patient's own hormonal cycle is monitored, or in a medicated cycle using estrogen and progesterone to prepare the uterine lining**.**

4.3.1 In Endometrium Preparation there are several stepsare followed during FET cycle.

4.3.1.2 Hormonal replacement treatment (Programmed Cycle - PC):

In the HRT cycle, suppression of follicular growth, endometrial proliferation and subsequent secretory transformation is achieved by the administration of exogenous estradiol (E2) and progesterone (P4)

This preparation method was developed for patients who had ovarian failure in the context of an oocyte donation program but has now become the most widely used protocol to ensure endometrial preparation before FET. Because the exogenous administration of estrogens suppresses follicular growth, pregnancies established after PC-FET miss a functional corpus luteum and consequently lack vasoactive substances such as relaxin, which are important for early maternal cardiovascular adaptation, produced by the latter .

- **Estrogen supplementation:**

Estrogen supplementation is the initial step in the HRT Cycle of endometrial preparation in this process from second or third day of the cycle to prime the endometrium and suppress spontaneous follicle growth. Estradiol is administered either at a fixed constant dose (6 mg daily) or most commonly used is 2 mg/day during days 1-7, 4 mg/day during days 8-12, 6 mg/day during days 13 to embryo transfer.

Different routes, including oral (micronized estradiol or estradiol valerate), vaginal (estradiol valerate) or transdermal (estradiol gel), can be used for the administration of E_2 with comparable reproductive outcomes.

Usually, after 12 – 14 days of E_2 administration, vaginal ultrasound examination is performed for endometrial thickness measurement and to confirm the absence of a leading follicle.

When the endometrial thickness >7 mm, P_4 supplementation is commenced, and timing of FET is scheduled accordingly.

Progesterone is continued after FET till 9 week if it day 3 embryo transfer or 12 weeks if its day 5 (Blastocyst stage).

To conclude, in HRT cycle, E2 priming with oral or transdermal routes has similar efficacy. The optimal duration for E2 priming is between 10 to 36 days, which offers a greater flexibility of timing of FET without compromising reproductive outcomes. Although pituitary suppression with GnRH-agonist decreases the cycle cancelation rate, HRT without suppression is more patient friendly and is associated with similar CPRs when compared with those attained with GnRH-agonist suppression.

4.3.1.4 Natural Cycle (t-NC)

It is a unstimulated spontaneous cycle ,single Oocyte is used in this procedure with no medication given to the patients.

t-NC is most optimally performed in patients with regular menstrual cycles. In t-NC, to schedule FET, the timing of spontaneous ovulation needs to be tracked theday of ovulation is crucially important in t-NC and will rely on documenting the LH surge and signs of ovulation. , The LH surge can be tracked by using Ovulation Kit or by testing in the blood serum rather than urine.

It is necessity to frequently observe the endocrine and follicular growth under the guidance of transvaginal ultrasonographic monitor . Hence, NC is less flexible when compared with HRT and modified-NC. In modified-NC, triggering is performed when the leading follicle is between 16-20 mm in diameter and scheduling is performed accordingly; modified-NC requires less endocrine and ultrasonographic monitoring when compared with t-NC and, thus, is considered more patient-friendly.

For t-NC, transvaginal ultrasonography is performed on day 2 or 3 of menses to rule out any cyst or corpus luteum prevailing from the previous cycle.Transvaginal ultrasonographic monitoring is usually started on day 8-10 and endocrine monitoring is performed, using serum E2, LH and P4 measurements when the leading follicle attains a mean diameter of approximately 15 mm in diameter. Following frequent endocrine and ultrasonographic monitoring, on alternate days or dyail, the day of ovulation is precisely documented to schedule the timing of FET.

4.3.1.5 Modified Natural cycle – (Modified- NC)

This is the semi-natural , Controlled natural cycle IVF. Single Oocyte is used and HCG is given to patient FSH/HMC given again .

For modified-NC, the initial monitoring is the same as in t-NC; however, ovulation is triggered with hCG once the leading follicle reaches a diameter of 16-20 mm. In modified-NC, hCG, not only induces ovulation, but also results in increased serum P_4 production during the early and mid-luteal phase, thus, the hCG trigger works as an ovulation trigger as well as an early LPS-luteal phase support.

In theory, the lowest effective dose to induce ovulation will result in a lower early serum P4, which should reduce the risk of endometrial advancement, known to have a negative impact on endometrial receptivity.

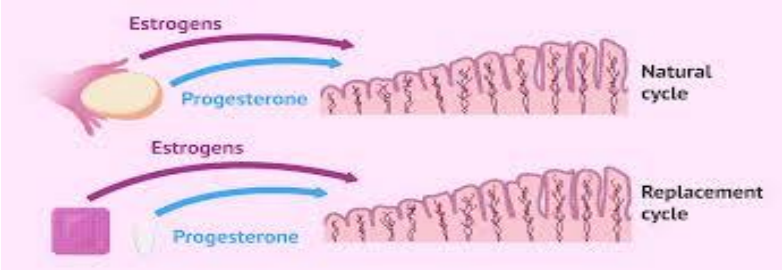

Fig 12 : Comparative of Natural and HRT

AdaptedFromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fnatural-cycle-of-embryo-transfer%2Fnatural-vs-replacement-cycle%2F&psig=AOvVaw1eg2vcTJTSG_U2_FXHvB2z&ust=1717493231414000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwjFlvyAj7-GAxUHZmwGHQiVAp0QjRx6BAgAEBQ.

4.3.1.3 Mild-Ovarian Stimulation (mild-OS)

A minmal amount of stimulation is used in this is cycle , it is friendly IVF. 2-7 Oocytes are used in tis procedure low dose of FSH /HMG oral compounds and GnRh is given to patients

Exogenous gonadotropins may be used to prime the endometrium for FET.

In this mild OS is performed with <150 IU urinary/recombinant follicle stimulating hormone (FSH)/day, letrozole at a dose of 2.5 – 5 mg/day.starting on the 2nd or 3rd day of the cycle. The follicular response is monitored frequently with the help of vaginal ultrasonography .

GnRh is administered when the diameter of the leading follicle is greater than17 mm, endometrial thickness ≥7 mm and serum E2 level >150 pg/ml.

After 36hrs of OPU Progesterone (P_4) is given.

The timing of the FET is scheduled according to the day of embryo freezing; day-3 embryos are transferred on hCG+5 and day-5/6 embryos are transferred on hCG+7.

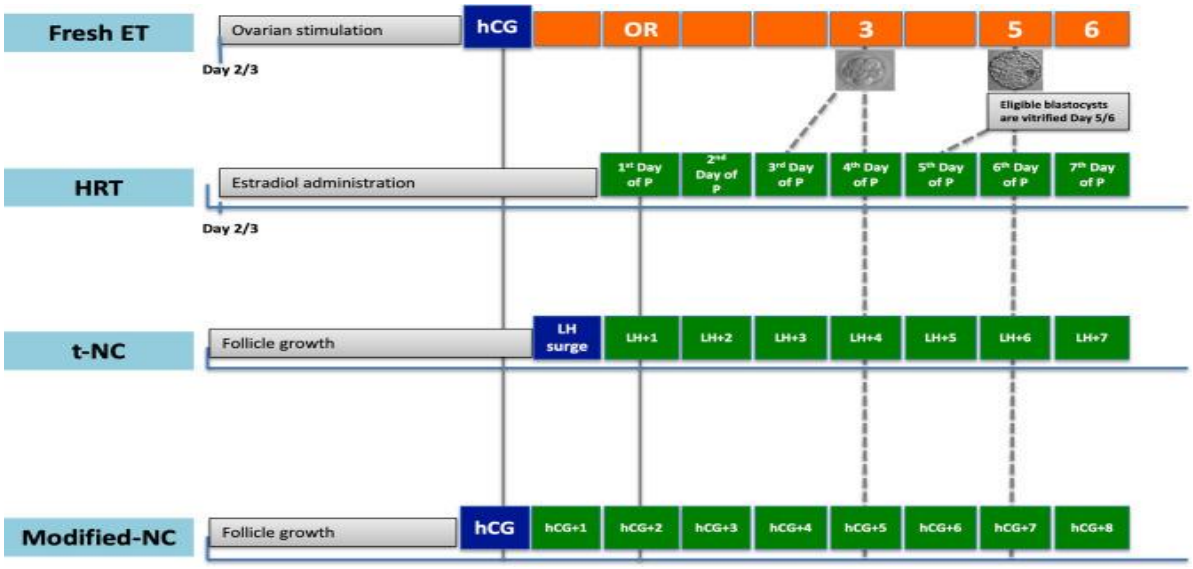

Fig 13 : Overview of Endometrium preparation in FET

AdaptedFromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.frontiersin.org%2Fjournals%2Fendocrinology%2Farticles%2F10.3389%2Ffendo.2021.688237%2Ffull&psig=AOvVaw1PCrtjKH5EYRAJ5rsruz3s&ust=1717493174002000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwjJgszljr-GAxWhbmwGHT8WAsoQjRx6BAgAEBQ.

What are the benefits of frozen embryo transfers over a fresh (stimulated) cycle?

Genetic testing

A major benefit of FETs is that it allows for preimplantation genetic testing to take place. Genetic testing can look for chromosomal abnormalities that may lead to miscarriage or genetic disorders.

Less medication

Instead of stimulation medication, patients use estrogen and progesterone to thicken the lining of their uterus in preparation for the embryo transfer to allow implantation. Since the stimulation phase was done in a prior cycle, there is also no egg retrieval requiring anesthesia.

Less stress

FET cycles are often less stressful than fresh cycles because factors like stimulation response, egg development, and embryo growth were considered during the fresh cycle. Shady Grove Fertility only freezes high quality blastocyst-stage embryos, giving patients a significant chance of success with an FET cycle. Cycles are also more predictable with fewer cycle cancellations.

4.3.2.Monitoring:

Before the transfer the endometrium is tracked under ultrasonagraphy to check with the triple lining , Blood flow in 3/4th Zone & Periferial Blood flow this are major things observed before the Embryo transfer .

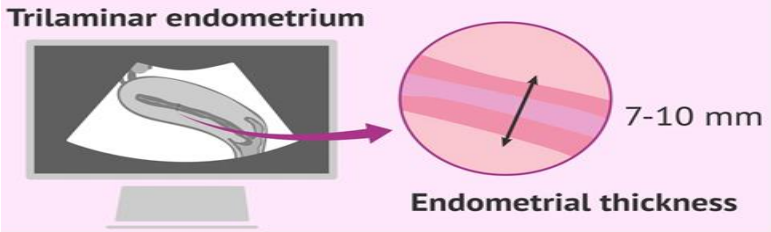

Fig 14 : Trilaminar Endometrium

Adapted Fromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.invitra.com%2Fen%2Fpreparation-of-the-endometrium%2F&psig=AOvVaw0gSKfouPctXZHXI-ILQa5S&ust=1717491010111000&source=images&cd=vfe&opi=89978449&ved=0CBIQjRxqFwoTCNDWxfaGv4YDFQAAAAAdAAAAABBW.

4.3.3Thawing of Embryos:

The embryo thawing is a process for recovering the physiological temperature of embryo and replacing the cryprotectant molecules with intracellular water .

The embryos are carefully thawed on the day of the transfer.

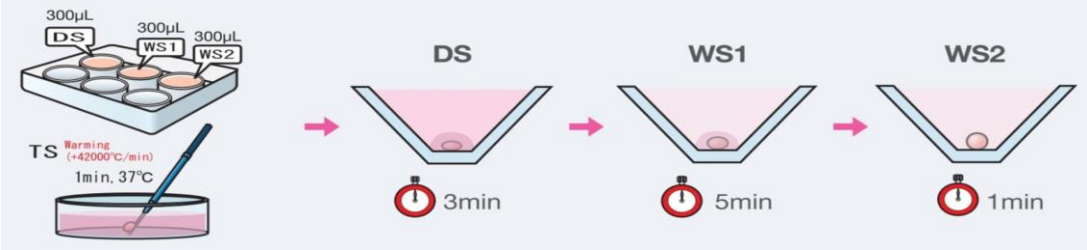

Fig 15: Thawing Process step by step

AdaptedFromhttps://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.planer.com%2Fdownloads%2Fkitazato%2Frecommended-usage-protocol-thawing-media%2F621-recommended-usage-protocol-thawing-media.html&psig=AOvVaw2ZJCxPEOSp_MmuXQmwgxho&ust=1717493102823000&source=images&cd=vfe&opi=89978449&ved=2ahUKEwiIztPDjr-GAxXUT2wGHdM9AWMQjRx6BAgAEBQ.

4.3.4 Embryo Transfer:

The embryo is placed into the uterus using a thin catheter. This is a quick and usually painless procedure.

Estrogen and progesterone supplementation continue after the transfer. Typically, a blood pregnancy test is checked 10 days after the embryo transfer. If you are pregnant, then hormone supplementation will continue until 10 weeks. If you are not pregnant, then your provider team will provide instructions to discontinue supplements in preparation for another cycle.

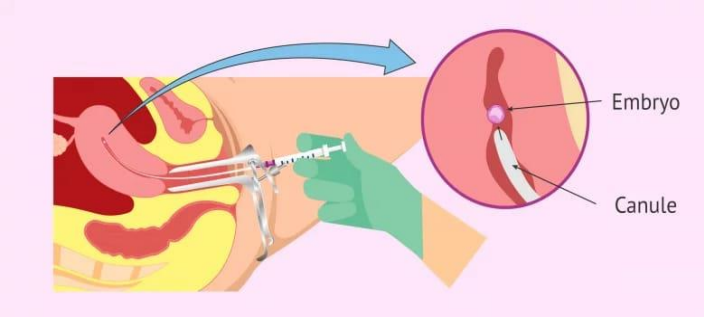

Fig 16 : Embryo Transfer

Adapted Fromhttps://images.app.goo.gl/GPhVCgJwqv3N2eoy5

4.3.5 Post-Transfer Care:

The patient may be advised to rest and take medications to support the uterine lining and embryo implantation.

Conclusion:

While both fresh and frozen ET have their merits and challenges, understanding their differential impact on endometrial preparation is crucial for improving the success rates of ART procedures. Further research into optimizing endometrial receptivity in both fresh and frozen ET cycles is essential for advancing the field of reproductive medicine and enhancing outcomes for patients undergoing fertility treatments.

Fresh ET involves the immediate transfer of embryos into the uterus during the same cycle as ovarian stimulation, while frozen ET entails the cryopreservation of embryos for future transfer. The timing of endometrial receptivity is critical for embryo implantation, and the differences in endometrial preparation between fresh and frozen ET can significantly influence the success of ART procedures.

In fresh ET cycles, the endometrium is often exposed to supra-physiological hormone levels due to ovarian stimulation, potentially compromising its receptivity. High levels of exogenous gonadotropins and ovarian hormones can disrupt the endometrial environment, leading to impaired implantation and decreased pregnancy rates. Additionally, the risk of ovarian hyper-stimulation syndrome (OHSS) is inherent in fresh ET cycles, posing further challenges to successful outcomes.

Advancements in ART continue to refine fresh embryo transfer techniques, enhancing the synchronization of embryo and endometrial readiness, and improving clinical outcomes. As a result, FET remains a widely used and continually evolving practice in the pursuit of successful pregnancies for couples facing infertility.

Conversely, frozen ET offers advantages in endometrial preparation by allowing for more controlled and personalized protocols. In frozen cycles, the endometrium can be prepared in a natural cycle, where hormonal fluctuations mimic the physiological conditions of the menstrual cycle, or in a hormonal regulated cycle with exogenous hormone supplementation.

This flexibility enables clinicians to tailor endometrial preparation protocols according to individual patient characteristics, optimizing the receptivity of the endometrium for embryo implantation.

Recent research indicates that frozen ET is associated with higher live birth rates and lower risks of OHSS compared to fresh ET. The ability to avoid the adverse effects of supra-physiological hormone levels and OHSS makes frozen ET an attractive option for patients undergoing ART treatments. Moreover, the option to bank embryos for future use provides patients with additional opportunities to achieve successful pregnancies, even after multiple cycles of ovarian stimulation.

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