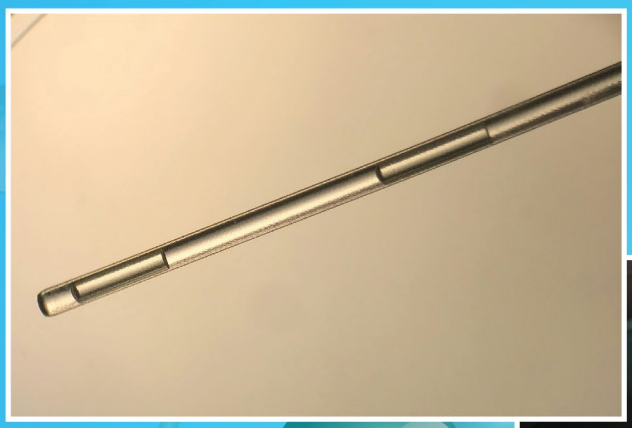
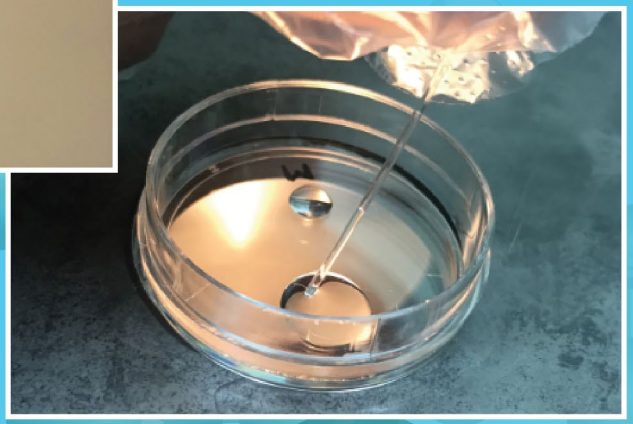
Volume 9 (Oct, 2018)

NEXUS

Indian Fertility Society & ORIGIO India Initiative

EMBRYO TRANSFER





Chief Editor
Dr. Pankaj Talwar

Dr M Gouri Devi
President - IFS

Embryo transfer is a simple procedure that is followed in In-vitro fertilization (IVF) and often considered the final step in the IVF process. The objective of embryo transfer is to facilitate conception following fertilization from the IVF procedure. It is the placement of an embryo(s) created through IVF into the recipient's uterus at the 2-8 cell stage. Embryos may be transferred at an early stage of development when they have few cells (cleavage stage), or in later stages of development when they have many more cells (Morula and blastocyst stages).

Many clinicians prefer blastocyst transfer as these embryos are more developmentally advanced, healthier, stronger and have a significantly higher rate of implantation when compared to Day three embryos. Therefore, we can transfer fewer number of embryos without reducing the chance of pregnancy.

In this issue we would cover the detailed steps involved in the Embryo Transfer and try to find answers to the complex unanswered questions.

Prof (Dr) Pankaj Talwar
Secretary General - IFS
Editor NEXUS

Dear all,
I thank all the readers for the overwhelming enthusiastic response towards the last Nexus. Your encouragement motivates us to present more advancements in the field of Assisted Reproduction Techniques. It justifies our commitment and the name "NEXUS" which means bridging gaps. As technologies, procedures and tools are evolving rapidly, we must adopt them and put them to use in order to reap full benefits. Nexus attempts to amalgamate already acquired knowledge and latest advancements.

In this bulletin of Nexus we are going to detail the technique of Embryo transfer (ET). ET is not only critical but also rate determining technique/procedure in the assisted reproductive domain.

Each step enmeshed in this procedure has its own importance, and we will be focusing on detailing the same. We will deep dive into the choice of embryo transfer catheters, as they need to be customized, depending on the negotiation of the cervical passage of the patient. In case of easy negotiation, soft catheters are most suitable while difficult transfer demands stiff catheters. Moreover, the volume of media used during embryo transfer is also significant. In the era of advancements, thin microvol catheters are ideal and are easy to handle requiring minimal amount of media for transfer.

We will delve into every aspect of ET and present the same in simple and easy to use information so that both beginners and experts are benefited. Our aim is to empower readers with the knowledge to improve their results. I hope you all will enjoy reading this and feel free to get in touch with us with any suggestions, as feedback always helps to improve.

I am thankful to guest editors for helping me in designing this piece of art. We would also like to express our gratitude to Origio India Limited who are helping us in the publication of this bulletin.

Jai Hind
M: +91 9810790063
E: pankaj_1310@yahoo.co.in

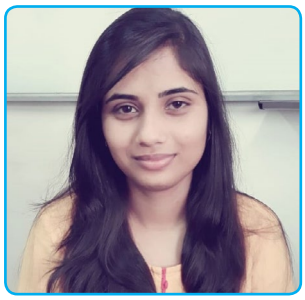
Guest Editors

Pooja Awasthi
Clinical Embryologist

Embryo transfer is the most crucial and rate-limiting step in the journey of Assisted reproduction. Cascade of factors plays a significant role in the successful Embryo Trsnsfer, starting from patient's physiological uterine environment like quantity of mucus, uterine contraction frequency, patient's medication, dose of progesterone, psychological health of the patients, choice of catheter and media, ultrasound guidance, embryo quality and last but not the least the technique of embryo transfer. Embryologists are the linchpin of the assisted reproduction. Inspite of having the latest technologies, implantation rates vary and are Low. Therefore, importance of following precise protocol needs to be emphasised among all the stake holders.

Embryo transfer starts with the visualization of the cervix followed by cleaning with saline/culture media. A soft catheter, loaded with embryo is then brought to the clinician. At every step, the confirmation of patient is of utmost importance. After insertion of the inner catheter into the outer catheter towards fundus, under ultrasound guidance (at the Mid Fundal point) contents of the catheter are expelled, and embryos deposited. Negative pressure throughout the procedure (from loading to deposition of the embryo) should be taken care of, to avoid embryo expulsion or any mishappening.

This nexus provides a complete review of the nuances of the technique to optimize the current scenario of embryo transfer and different catheters available in the market.



Sapna
B.Tech Biotechnology

Embryo transfer is an important part of the IVF process wherein the eggs fertilized in a lab are implanted into an uterus with the help of ET catheter. The embryo may be fresh or frozen, or may use biological eggs or donor eggs, both of which may have an effect on the chances of getting pregnant.

It's a crucial final step of an Assisted Reproductive Technology (ART) cycle, where accuracy and skill while performing an atraumatic technique dictate the success of the technique. Failures at the embryo transfer stage may be due to lack of good quality embryos, lack of uterine receptivity or the technique itself. Another factor that could possibly effect the chances of getting pregnant is the number of embryos transferred per IVF cycle. To decide this, several factors must be considered including age and medical history of the patient including previous IVF treatment, developmental stage of the embryos at transfer or quality and quantity of the embryos available for transfer. Embryo transfer is needed when there is ovulation disorder, damage to fallopian tubes, endometriosis, premature ovarian failure, uterine fibroids, genetic disorders or impaired sperm production

Through this bulletin we have tried to explain all the factors that influence the outcome of ET such as including uterine factors, embryo selection, timing, choice of catheter to name a few. It also includes comprehensive comparative charts on ET catheters which will help clinicians and embryologists to know the paralleling advancements to improve their results.

INDEX

Part - 1

Embryo Transfer : Basic concepts

SUB-INDEX

Part : 1
Embryo Transfer : Basic concepts

1 Introduction

Embryo transfer (ET) is the final and most crucial step in Assisted Reproductive Technologies in which the embryo is placed in the endometrium through the cervical canal. For a successful ET, a viable embryo, a receptive endometrium and a good ET technique are required. The embryo transfer technique has a great impact on the IVF results. It has been proven that the pregnancy rates differ significantly among different individuals performing ET within the same IVF program. ET was performed for the first time in 1978 and is still being fine tuned. A number of studies and improvements have been conducted in process for better and fruitful transfer of embryo. Regardless of advancements in ART, the rate of implantation is still low. Embryos transferred in to the uterine cavity can be expelled due to numerous factors including uterine contractions/ peristalsis, site of deposition, cervical mucus and negative pressure generated during ET.

2 Factors associated with ET Outcome

i. Uterine contractions
ii. Intrauterine lesions
iii. Cervical mucus
iv. Internal cervical os
v. Endometrium
vi. Mock Embryo Transfer
vii. Ultrasound: Its relevance before, during and after ET
viii. Type of media used in ET
ix. Type of catheters used in ET

i. Uterine Contractions

Generally, uterine contractions are due to the tightening and shorting of the uterine muscles. Uterine contractions at the time of ET are associated with a lower pregnancy rate. Initiation of uterine contractions may lead to an immediate or delayed expulsion of the embryos and has been considered a big concern in ART.

Prostaglandins present in the uterus play the pivotal role in contraction of smooth muscles of uterus and biophysical changes associated with it.

A study by L. Zhu et al. in the journal of Human Reproduction, March 2014 shows quantitative marker of uterine receptivity and pregnancy outcome in an embryo transfer cycle. Patients with uterine peristalsis of < 3.0 waves/ min before embryo transfer had a higher chance of pregnancy compared with those with higher frequencies. The clinical pregnancy rate was the highest when < 2.0 waves/ min were observed and it decreased with an increasing wave frequency.[1] Predictive validity of the cut-off value needs to be tested in further studies.

Approaches to inhibit Uterine Contractility before ET:

- Vaginal progesterone administration
- Cyclooxy genase inhibitors
- ß2-adrenoreceptor agonists
- Calcium-channel blockers
- Phosphodiesterase inhibitors
- Oxytocin antagonists

A study conducted in 2001 concludes that the administration of vaginal progesterone two days prior to embryo transfer significantly reduces the frequency of uterine contraction.[2]

ii. Intrauterine Lesions / Uterine Abnormality

- Polyps
- Myomas (fibroids)
- Synechiae
- Chronic Endometritis
- Uterine fluid

iii. Cervical mucus

The cervical mucus is a fluid secreted by the cervix, under the influence of estrogen. Throughout the menstrual cycle, the amount and quality of cervical mucus fluctuates. At the time of ovulation, the estrogen levels begin to surge, which causes cervix to secrete more cervical mucus. It acts as a marker for the fertile quality and provides nutrition to the sperm. After ovulation, the quantity of cervical mucus begins to decline and become thicker in consistency.

Potential concerns with cervical mucus present at time of ET include decreased transfer efficiency and increased incidence of retained embryos. Cervical mucus may by covering the catheter tip, causing the dragging of embryos and it can be a source of bacterial contamination of uterine cavity too.

There are studies which indicate that the, removal of cervical mucus during embryo transfer (ET) has no positive effect on the pregnancy rate.[3]

However, according to some reports, removal of cervical mucus during ET has been shown to increase the pregnancy and implantation rates by not interfering with embryo implantation. [4] It was found that cervical mucus culture tested positive in 71% of patients and 49% of patients had positive culture at the catheter tip and thus involved in reduced pregnancy rates. [5] [6] Several studies have shown that cervical mucus aspiration can decrease infection rate with E. coli, Mycoplasma, Uroplasma, Streptococcus B, D, Staphylococcus, thereby and increasing implantation rates.

Removal of cervical mucus - Removing the cervical mucus before ET is advisable in order to avoid the adverse effects mentioned previously. It can be removed by repeated gentle aspiration using a 1-cm^3 syringe with its tip placed at the external cervical os or using a soft catheter.

The endocervix can be cleaned of mucus using a sterile cotton swab or small brush and then small amounts of culture media. According to different scientific studies, vigorous cervical washing at the time of ET is not recommended as it is related to initiation of uterine contractions and poor implantation rates. According to a large retrospective study including 470 ET procedures, it was reported that the presence of microscopic blood and mucus did not affect the clinical pregnancy or implantation rates. [7] According to Cochrane review, no evidence of benefit was found when the cervical mucus was removed before ET. [8]

iv. Internal cervical OS

The internal orifice of the uterus is an interior narrowing of the uterine cavity. It is crucial for a successful ET that the catheter passes through the cervical canal and internal os to enter the uterine cavity. Soft ET catheters can pass through internal os easily if the uterus position is normal. The reason behind the failure of a catheter to pass through internal cervical os is the lack of alignment between the straight ET catheter and the curved or acutely angulated utero-cervical angle. The most common reasons for difficult transfer are acute degree of anteversion/retroversion or utero-cervical angulation and cervical stenosis. Distorted anatomy with fibroids, previous surgery, or congenital anomalies may lead to very difficult ET.

v. Endometrium

The endometrium is the inner lining of the uterus. Each month, the endometrium thickens and renews itself, preparing for pregnancy. Endometrial thickness (EMT), measured in the sagittal plane by transvaginal ultrasound and expressed in millimeters, and is routinely assessed in patients undergoing for IVF treatment.

Adequate endometrial development is required for pregnancy to occur. The pregnancy rates were found to be higher when the endometrium reached at least 9 mm thickness with a triple line pattern. Other prognostic factors, such as embryo quality and age, are taken into consideration. A markedly thick endometrium deters implantation. Likewise, the endometrial volume, measured with 3D ultrasound, of less than 2.5ml on the day of transfer showed poor probability of implantation.

Damage to the Endometrium

Injury caused by tricky embryo transfers due to cervico-uterine angulations or the lack of experience by the clinicians may disrupt the endometrium with a consequent negative impact on the endometrial receptivity and implantation rates. [9]

Injury may lead to:

- Bleeding in the uterine cavity
- Inflammatory changes in the endometrial lining
- Plugging of the embryo transfer catheter, which in turn may retain the embryos leading to Grade 2 transfer
- Initiation of uterine contractions, which eventually may expel the embryos from the uterine cavity
- The damage may be avoided by thorough clinical assessment of the care before actual embryo transfer.

vi. Mock Embryo Transfer

A mock ET before the start of the IVF cycle has been shown to improve the pregnancy rate significantly. During the mock ET, we can measure the length of the uterine cavity and evaluate its direction and the degree of cervico-uterine angulation. Mock ET can be performed –

a) A month before the actual IVF cycle (mid luteal phase)
b) At the time of oocyte retrieval
c) 3 to 5 days before ET.

No deleterious effect on the endometrium has been seen while doing mock ET. It is also useful for choosing the most suitable kind of catheter. The presence of any congenital anomalies or any unanticipated difficulty like presence of polyps or fibroids, pinpoint external os, and stenosed cervix from previous surgery can also be discovered. It is advisable to perform cervical dilatation before starting the IVF cycle in cases of cervical stenosis. Cervical dilation should be performed one month before the IVF cycle with the use of cervical laminaria. Studies have reported, very low pregnancy rates with dilatation done at the time of ovum pick up.

vii. Ultrasound : It's relevance before, during and after ET

a. Before ET

Ultra-sonography is an essential part of embryo transfer to measure and evaluate the uterine cavity, cervico-uterine angle, depth of endocervical canal and its orientation before ET.

- **Uterine orientation:** A study on uterine orientation in 2004 have concluded that a retroverted uterus at mock ET, is more likely to change at the time of actual ET; while if the uterus is anteverted, it is more likely to stay in the same position at the time of real ET. [10]
- **Cervico-uterine angle:** The estimation of the utero-cervical angle, allows to find the direction of the catheter along the contour of the endometrial cavity. It avoids disruption of the endometrium, plugging of the catheter tip with the endometrium and instigation of bleeding. Patients with large angles (>60°) had significantly lower pregnancy rates compared with those with no angle. [11]
- **Depth of endocervical canal:** The estimation of cavity depth by ultrasound helps in determining the depth beyond which catheter insertion should not occur. ET under ultrasound guidance enables the transfer of embryos into the uterine cavity at a fixed distance from the fundus (difference between the cavity depth and depth of catheter insertion). This significantly increases the chances of clinical pregnancy, embryo implantation, ongoing pregnancy and a live birth. The authors have reported the benefit of depositing embryos at a distance of >1 cm from the fundus. Several studies reported that the distance between 1-2 cm seems to be the best site for ET to get higher pregnancy rates. A Cochrane review of 17 RCTs showed that US-guided ET increased the ongoing pregnancy rates compared with clinical touch. [12]

b. During ET

- Transabdominal ultrasound-guided embryo transfer offers the clinician an opportunity to visualize the echogenic tip of the catheter and decide the exact site of embryo deposition.
- Avoids injuries to the fundus.
- May facilitates a smooth access through the cervices to the uterine cavity, thus overcoming the chances of cervical stenosis.
- Ultrasound may be useful in difficult cases to visualize the uterocervical angle to negotiate the catheter accordingly in order to minimize trauma to the cervical canal and/or the endometrium.
- Benefit of this technique as compared with clinical touch transfer has been shown in a meta-analysis of Buckett. In contrast, a recent randomized study could not confirm this finding. [13]

c. After ET

Ultrasound also ensures that the embryo air bubble interface is not displaced after ET.

viii. Type of media used for embryo transfer

Embryos should be transferred in any media with high protein content in physiological concentration, which has similar milieu to the uterus on the day of implantation. Wide variety of macromolecules like fibrin sealants and hyaluronan (Embryo Glue) have been suggested to improve the implantation rate. RCT found that treating the embryo with fibrin glue (Embryo Glue) prior to ET resulted in a significant improvement in clinical, implantation, and ongoing pregnancy rates. We do day 2 embryo transfer in G2 (Vitrolife)/Cleavage media (Cook) pre-equilibrated media. Single step and sequential, both type of media can be used and depends upon embryologist's choice. **Hyaluronan - enriched** transfer medium can improve the clinical outcome, especially in patients with poor prognostic features.

[**Hyaluronic acid** is a glycosaminoglycan molecule with a strong negative charge thus, it attracts volume of water. This hydration produces a viscous solution, which might facilitate embryo transfer and prohibit, expulsion of the embryos. Interaction of Hyaluronic Acid with CD44 molecules, expressed on human embryos and on the endometrial stroma acts as a hub connecting the two.]

ix. Type of catheters used in embryo transfer

- The ideal ET catheter should be safe, user friendly and soft enough to avoid any trauma to the endocervical canal or endometrial cavity.
- It should be easily visible under USG vision.
- It should be pliable enough to negotiate through the cervical canal into the endometrial cavity.
- Additionally, its tip should be smooth and non-traumatic to the lining of endometrium.
- Ideal catheters are of co-axial variety. The outer sheath should also be malleable and inserted till internal os very gently.

Most ET sets available in market are composed of an outer sheath and an inner catheter. An outer sheath is used for cervical canal negotiation and an inner catheter is used to load the embryos. The inner sheath is introduced to endometrial cavity through the lumen of the outer sheath. The ET catheters are made of polyurethane or polyethylene (non-embryo toxic plastic). Generally outer sheath is made of polycarbonates but some are of polytetrafluorethylene. The use of natural rubber latex in the ET catheters should be prohibited as it can trigger allergic reactions.

There are few one-piece ET catheters such as the Semtrac C (Gynetics, Lommel, Belgium) in the market. ET catheters vary in material, length, calibre, degree of stiffness, and echogenicity of the inner catheter as well as malleability and design of the outer sheath, i.e., curved or straight, with or without a bulb tip.

a. Soft ET Catheters

Various models of soft ET catheters are in market and used routinely such as Wallace® (CooperSurgicals, Origio o/s, knardrupuejz IVOSLOV Denmark), Frydman (Laboratoire CCD, Paris, France), and Cook (Cook Ob/Gyn Inc., Bloomington, IN, USA). Catheters, which are specifically designed to be used in the "outer sheath first" fashion, are the most recent. These include the Labotect (M) (Goettingen, Germany) ET catheter, all models of Kitazato (Shizuoka, Japan), Cook Sydney IVF and Guardia Access ET models. These ET catheters have a slightly curved outer sheath to fit the natural curve of the cervical canal, and there is a small bulb at the tip to facilitate negotiating cervical crypts and the internal ostium.

Systematic reviews and meta-analyses of 10 studies comparing soft ET catheters with more rigid ones done by Abou-Setta AM and Buckett WM reported the use of soft ET catheters is associated with significantly higher clinical pregnancy rates. [13, 14]

The reason behind high pregnancy rate associated with soft catheters is unclear; however the possible logical reason could be less trauma to the endometrium. Despite being less traumatic, the risk of failure to negotiate the cervical canal is higher with soft catheters. Difficulty in negotiating the cervical canal with a soft catheter led to the use of a tenaculum or stylet or sounding the uterus more often than firm catheters. Therefore the choice of right catheter is very important for embryo transfer.

b. Firm ET catheters

Firm catheters such as the Tight Difficult Transfer (TDT) catheter (Laboratoire CCD), Rocket (Rocket Medical, Watford, England) and Emtrac-A (Gynetics) are available in the market. Despite the use of similar material, these catheters have firmer inner catheters than those of the soft models, and therefore, are considered as "firm" ET catheters. Some physicians prefer to use a firm catheter routinely, most would reserve them for technically difficult transfers, e.g., in the presence of a convoluted or stenotic cervical canal.

c. Echogenicity of ET catheters.

Echogenicity is the ability to bounce an echo. ET under ultrasound guidance has led to the production of ET catheters with increased echogenicity.

Two different techniques are used to increase echogenicity of ET catheters. The more commonly used technique involves integration of a metal ring close to the tip of the inner catheter. Examples include Kitazato catheters, Cook Echotip, and Rocket EchoCat series. The metal ring is <2 mm and only provides increased echogenicity toward the tip.

On the other hand, the SureView® series by CooperSurgical Origio is unique in providing increased echogenicity through the entire length of the inner catheter. This is achieved by mixing air bubbles into the material. Echogenic catheter can be more important for less experienced physicians and can be more advantageous for a selected group of patients, e.g., obese women or women with a retroverted uterus.

x. Gentle and atraumatic technique used during embryo transfer

The embryo transfer should be atraumatic, painless and gentle, characterized by the lack of blood, mucus, endometrial cells on the catheter tip, suggestive of injury to the endometrium. Even the insertion of the vaginal speculum should be done gently as it can initiate uterine contractions. Nearly 30% of embryo transfers may be difficult thus reducing the chance of conception. [15]

a. Choice of Surgical instruments for cervix manipulation during ET:

- **Cusco's speculum:** Cusco's speculum is recommended to be used in all embryo transfers as this makes the procedure atraumatic and gentle. Holding the cervix with a **vulsellum** during ET was found to increase oxytocin release and junctional zone contractions which remain high till the end of the procedure and can lead to the expulsion of the embryos. [16] Vulsellum should be used only in order to negotiate the cervical canal angulation with the catheter tip where necessary.

3 Experience of the Clinician and Embryologist

Non-traumatic embryo transfer avoids uterine contractions & influences the final outcome depending upon technical skills of the clinician. It is likely that the clinician's experience has an influence upon the outcome. The result of ET depend upon.

- Morphology and metabolism of the embryos
- Time interval between loading and transfer
- Choice of media and amount of media used during loading
- How much pressure is required on plunger during transfer, which depends on the skills and experience of an embryologists. [17]

4 Embryo grading and selection

Many studies have shown that morphological contents in the embryo can be used as biomarkers of quality and for superior embryo selection which may enhance pregnancy rates and potentially reduce further the number of embryos needed for transfer. A recent Cochrane review stated that delaying transfer from day 2/3 to the blastocyst stage (days 5–6) may offer a window of opportunity to select better quality embryos and gives better pregnancy rate. The embryo quality can be assessed by various methods.

a. Morphology of embryo

Mostly scoring systems are based on several morphological parameters such as:

- Cleavage stage
- Embryonic fragmentation
- Blastomere uniformity and number.

The newer techniques, such as time-lapse, PrimoVision, and Miri® TL provide multilevel digital recording of embryo images and software programs that allow detailed interpretation of the embryo quality/morphology. Data collected from these techniques does not compromise the embryo quality, that would occur as a result of increased handling time outside the incubator.

b. Embryo metabolics

Micro methods for assessing the metabolism of embryos were developed in order to improve the selection of embryos with the best developmental potential. These include the:

- Embryos' respiratory rate
- Glucose consumption
- Nitric oxide levels
- Amino acid turnover pace.

These techniques are cumbersome and are in experimental stage.

5 Duration of ET

The prolonged exposure of embryos to ambient temperature, light, humidity or other factors can be detrimental for them. Therefore the time interval from loading the embryos in the catheter to depositing them in the uterine cavity should be kept to a minimum. More than 1 minute or 2 minutes time has been shown to lower the pregnancy and implantation rates. Although, contradictory studies showed no adverse effect in the duration of the procedure on the results if transfer takes up to 7.5 minutes [18]

6 Relevant issues related to be addressed post - embryo transfer

i. **Bed rest after Embryo Transfer:** Recent studies have shown that this is not necessary and that immediate ambulation following the ET has no adverse effect on the pregnancy rate as compared to bed rest for one to two hours.[19]

ii. **Sexual intercourse post transfer:** Large number of studies has revealed that the pregnancy outcome does not differ between the couples who avoided and those who did not avoid intercourse during the peritransfer period. [20]

iii. **Medication after transfer:** Routine use of low dose aspirin, sildenafil and antibiotics have not been recommended by any RCT. Progesterone is beneficial but starting its administration on the day of pickup did not have additional improved pregnancy rates as compared to starting it on the day of ET. [21] Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the production of prostaglandin. Administration of 10 mg of piroxicam one to two hours before the procedure demonstrated significant improvement of implantation and pregnancy rates. [22] Administration of 10 mg diazepam to ally anxiety, 30 minutes to 1 hour before the procedure, did not reveal any statistical difference in the outcome.

iv. **ET technique and Ectopic pregnancy:** The risk of ectopic pregnancy following IVF was estimated to be 5% in a multicenter study of 1163 pregnancies. (23) In a recent review, the prevalence of ectopic pregnancy secondary to ART ranged between 2.1% and 8.6% of all pregnancies. (24) This figure is much higher than in natural conception. The distance from the fundus to the tip of the ET catheter was studied in relation to the ectopic rate. The authors reported a decrease in the ectopic rate when the distance between the fundus and the tip of the catheter was increased. Another technique of mid-fundus deposition of embryos has also resulted in a lower percentage of ectopic pregnancy and did not negatively affect the pregnancy rate (25).

Ectopic pregnancy was 3.9 times more associated with difficult ET than with an easy procedure. (26) Another factor in the etiology of ectopic pregnancy in IVF is the size of the uterus. It was accounted that the ectopic pregnancy rate was essentially higher in women with endometrial cavity lengths of < 7 cm. The ET technique can likewise be a reason for ectopic pregnancy because of forcing the embryo(s) through tubal ostia by hydrostatic pressure or by utilizing more volume of ET medium. The speed of the transfer was additionally implicated in inducing ectopic pregnancy and was prescribed to be performed gradually over 10 seconds. At last, it was inferred that the uterine contractions are by and large cervico-fundal in origin in the early luteal stage and might be the reason for some ectopic pregnancies in IVF. As a result of uterine peristalsis, the embryos could move as easily toward the cervical canal as toward the fallopian tubes.

v. **Infusion of hCG:** hCG is a key molecule for the transplantation of the embryo. hCG effectively modulates several metabolic pathways within the deciduas contributing to endometrial receptivity. It was recently published that intrauterine infusion with 40 µl of tissue culture medium containing 500 IU of human chorionic gonadotropin (hCG) significantly improved the clinical pregnancy rates and implantation rates [27]. Confirmatory results of various RCTs are conflicting, some were in favour and others not. The conflicting results in the literature could be due to the variable degrees of purity of hCG, and the use of recombinant hCG could avoid such problem. It could also be due to variable days of ET ranging from day 2 to 5. Moreover, hCG is a fragile molecule and it should be prepared immediately before its use and not kept overnight in the incubator.

Part - 2

Protocol followed at our centre

INDEX

Part : 2
Protocol followed at our centre

1 Step by step embryo transfer procedure

i. Counselling: The patient is informed of the fertilization rate, the number of available embryos, and the number of embryos selected for the transfer. We transfer two embryos (4-6 cell stage) or single blastocyst during the procedure. Spare embryos are graded and patients are informed about the embryo's being frozen. All the communications are done as per Indian Council of Medical Research (ICMR) guidelines and patients are appropriately counselled.

ii. ET Procedure:

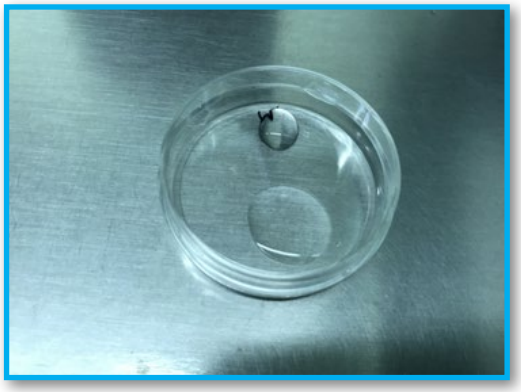


Fig : 4.1

Fig. 4.1: Preparation of the embryo transfer media plate. We use 35 x 10 mm tissue culture dish for the procedure. Embryo transfer is done at 4-6, cell or at blastocyst stage. Dispense small drop of G1 PLUS/ fertilization media /cleavage media at the top of the dish for rinsing of embryos to remove the traces of oil and is marked as 'W'. Another 300 µl drop of cleavage media / blastocyst/embryo glue/embryogen media is dispensed in the centre of the same dish. The media is equilibrated for minimum 8-10 hrs before dispensing and the plate is prepared minimum 30 minutes before the embryo transfer.

Fig : 4.2

Fig. 4.2: Day three, grade 1, 8-cell embryo. We prefer to carry out single embryo transfer in young patient and freeze the supernumerary embryos; this embryo is presently in cleavage media and is planned for embryo transfer.

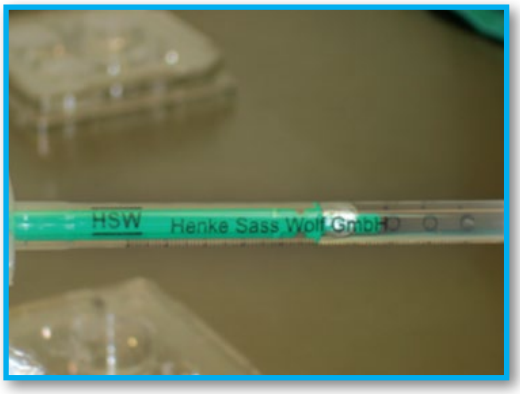


Fig : 4.3

Fig. 4.3: 1 ml syringe, without rubber plunger is used for embryo transfer. The nozzle of the syringe is attached to the embryo transfer catheter. We fill the syringe with 500 microliters of embryo transfer media—either blastocyst or embryo glue for flushing the catheter. Ensure that the syringe does not contain any air bubbles. Syringes are loaded with transfer media 30 minutes before the embryo transfer and kept in incubator for equilibration

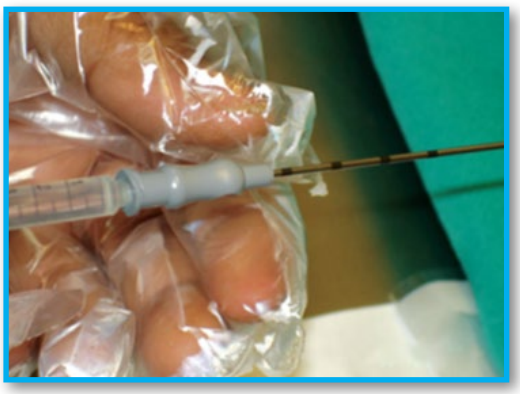


Fig : 4.4

Fig. 4.4: Now we attach the 1 ml syringe with the inner soft embryo transfer catheter. Ensure that the fitting is tight otherwise the assembly may detach at the critical period of flushing the embryo transfer catheter.

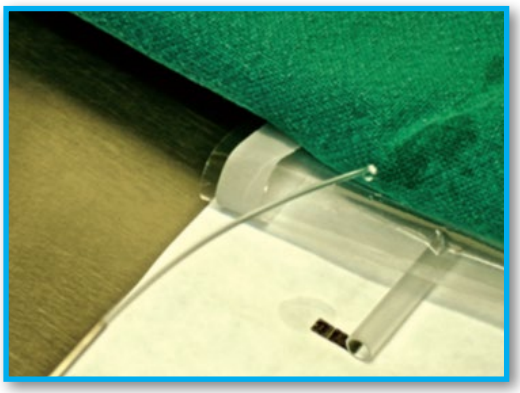


Fig : 4.5

Fig. 4.5: Inner soft embryo transfer catheter being flushed with the media. This will equilibrate the inner lining of the ET catheter with the media column loaded with the embryos. This avoids sudden shock to the embryo. The syringe should be flushed with similar media in which we transfer the embryos

Fig : 4.6

Fig. 4.6: Embryos are selected from the cleavage drop and the ones planned for the transfer are moved from cleavage plate to a small drop of G1 Plus / vitromed / fertilization media for rinsing and removing the traces of oil. These are quickly moved to a 300 µl drop of cleavage media/ blastocyst/ embryo glue media in the center of the same dish. The selected embryo/embryos are placed in the middle of the drop and brought into focus using a stereo zoom microscope at low magnification. These are now quickly loaded in the inner soft catheter in minimal volumes of the media.

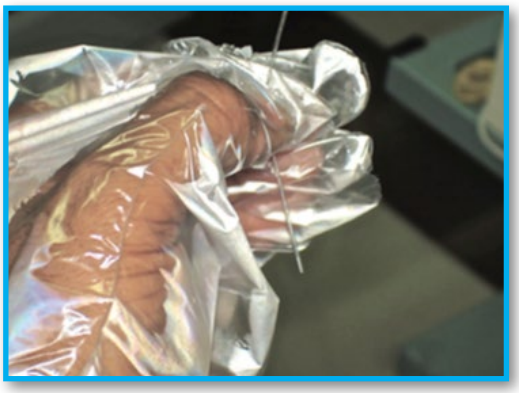


Fig : 4.7

Fig. 4.7: Soft catheter loaded with the embryos should be handled carefully. Gloves should be worn and the catheter tip should be kept horizontal. The catheter tip should be kept cupped to avoid exposure to the cold air currents.

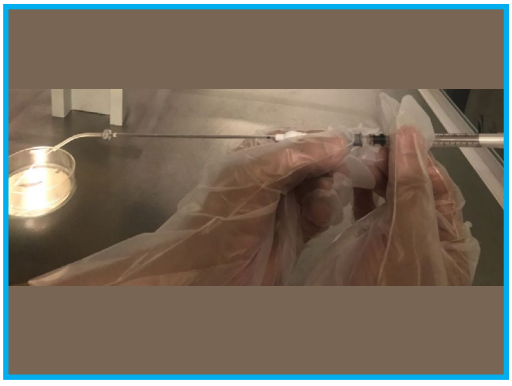


Fig : 4.8

Fig. 4.8: After the embryos have been transferred, the catheter is handed back to the embryologist. The catheter should be kept horizontal and cupped. Now the syringe is gently removed and media is allowed to flow on a clean warm plate

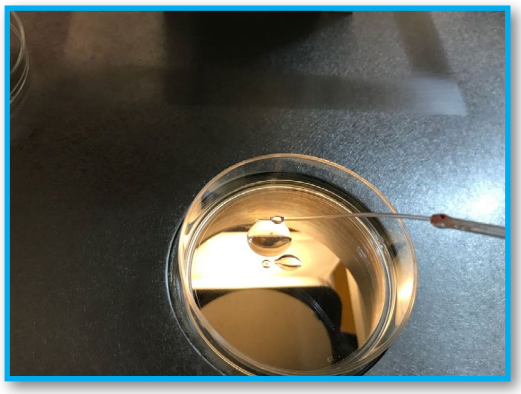


Fig : 4.9

Fig. 4.9: Returning media is observed for the retained embryos. The catheter tip is rolled on the plate to release any entrapped embryos on the catheter tip. Check the mucus plug for entrapped embryos. If retained embryos are seen these are transferred back to the cleavage media, equilibrated for 15 minutes and transferred again.

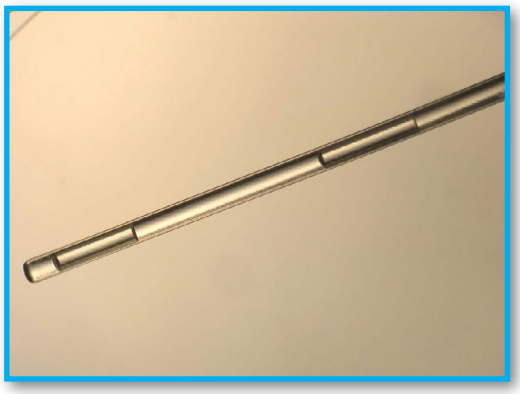


Fig : 4.10

Fig. 4.10: A close up view of the tip of the soft embryo transfer catheter.

iii. Ambient conditions for Embryo transfer

a. **Air quality:** Air quality has been and will always be a critical factor to address in the IVF laboratory. Developing a systematic process to control air quality will eliminate one of the major factors that affect the IVF outcomes. Air filtration systems, particle counting, VOC testing and pressure monitoring are a few of the ways in which one can control for its variable.

b. **Temperature:** Temperature is another very critical factor. Temperatures a few degrees below core temperature are less critical because of the cell's ability to slow its metabolism. However, temperatures a few degrees above core temperature can cause irreversible damage or death of the cell. Therefore, it is imperative that temperatures be maintained within tight range and that the instruments used to measure these temperature be extremely accurate (± 0.1°C).

c. **CO_2 level:** For 90% or more of the embryos to reach blastocyst stage, the CO_2 level had to be between 5 to 6% or depending upon the media used.

d. **Cleaning and Sterilization:** Sterilization of disposables that contact culture medium, gametes and embryos should not be overlooked. Improperly sterilized items or items not sufficiently aerated or rinsed prior use can affect the IVF results.

e. **Labeling of disposables:** All disposables should be labeled with unique patient ID.

iv. Preparation of Transfer Plates

a. **Sequential Media**

Culture plates (Falcon / Nunc) are prepared 2 hrs before the embryo transfer.

Different media have different working pH, at which they perform best, so gassing of media should be done accordingly. Vitrolife media work best at pH of 7.27, Cook at 7.3-7.5, Sage media at 7.27-7.30, and Irvine at 7.28-7.32.

Plate 1: Washing drop (W): Dispense a small drop of pre-equilibrated G1 media (Vitrolife) / Cleavage media (cook) at the top of the tissue culture plate.

Plate 2:Transfer drop: Dispense 300 µl of pre-equilibrated G2 (Vitrolife) / Cleavage media (COOK) media in the centre of the same culture plate.

- **Visualization and embryos grading:** Embryos are initially seen at 10 X – 20 X magnifications in a single well plate. After that the magnification should be increased to 40 - 50 X for segregation and grading of embryos.

Tip: Working at low light gives better results although it is strain on the eyes.

- **Transfer of embryos to dish:** 170 microns flexipet is used to transfer embryos from the cleavage plate to the transfer dish which contains G1 (Vitrolife) / Cleavage media (COOK).

  We must rinse the embryos gently in washing drop (W) to remove all traces of oil and old culture media. Here, we must work at low magnification and light as grading has been carried out already before shifting the embryos. Transfer drop contains more physiological media and will now act as our reservoir for embryo transfer and spare embryos.

- **Selection of embryos for transfer:** The top 2/3 embryos are selected and further transferred to the transfer drop. Embryos are loaded from this drop in G2 (Vitrolife) / Cleavage media (COOK) as they are physiological more akin to the uterine milieu.

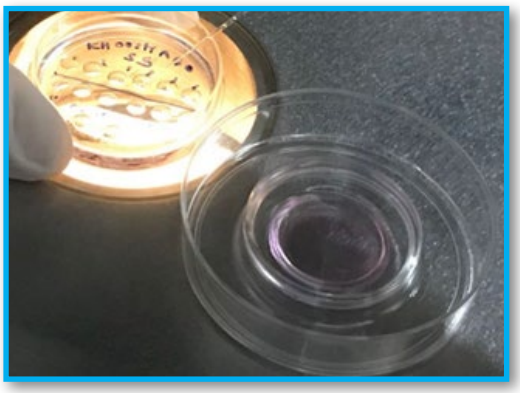
- **Cryo-freezing:** The balance of the embryos in transfer drop are vitrified.

b. Single Step Media

In case of single step media, shifting of embryos is required only once.

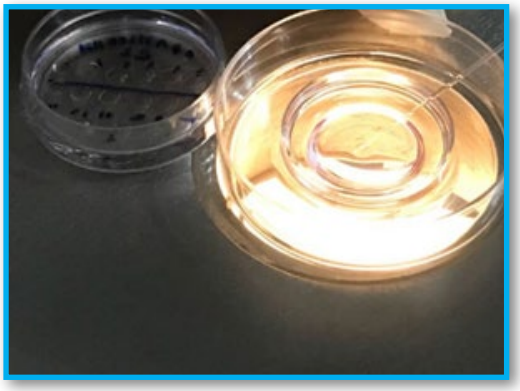
Central well plates (Falcon / Nuncs) are prepared just before the embryo transfer with pre-gassed one step (SAGE) / CSCM or CSM-NX (Irvine Scientific) / G- TL (Vitrolife) media.

- **Visualization and embryos grading is same regardless of type of media used.**



- **Transfer of embryos from culture dish to central well:** Selected embryos are transferred to the central well containing 1 ml of pre gassed single step media just before the embryo transfer.

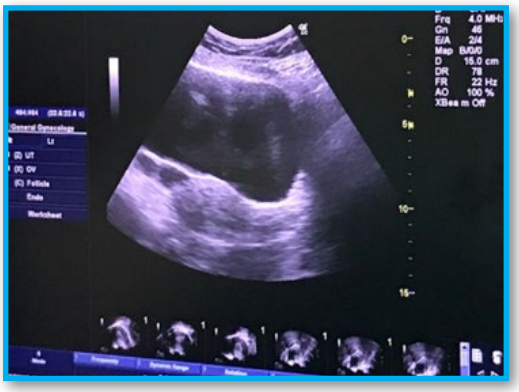
- **Cryo-freezing:** The balance of the good quality embryos in the culture dish are used for cryo-freezing.



v. Patient Preparation for Embryo Transfer

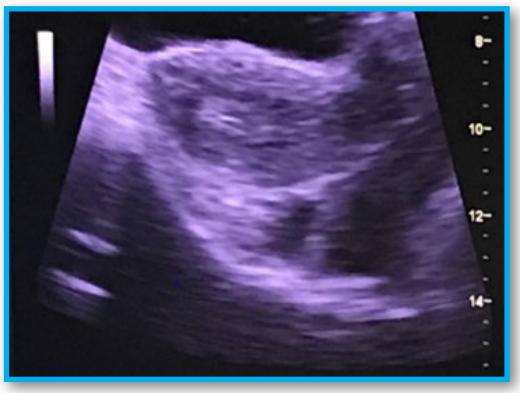
Pre - procedure Preparation: Number of variables affects ET in patients undergoing for ART. These factors should be taken care of before taking the patient for ET procedure.

a. **Pre-procedure medication:** We administer 10 mg diazepam injection intramuscular with 0.6 mg atropine intramuscular 1 hr before the procedure. If the patient is much stressed, it is better to perform ET under general anesthesia. (*ET under GA has low PRs as per the studies and should be avoided if possible)
b. **Fluid intake:** The patient is advised to drink fluids and inform the nurse when her bladder is full.
c. **Ultrasound for bladder status:** Check the status of the bladder before taking the patient to the embryo transfer room. We prefer bladder to be filled till the fundus of the uterus, so as to get satisfactory acoustic window during embryo deposition.



Ideal bladder distension before embryo transfer as seen on ultrasound

d. **Records:** The previously taken ultrasound picture of the uterus and the dummy ET is revised to get an idea about the length and direction of the uterus and the degree of cervico-uterine angulations.
e. **Position of the patient:** Put the patient in the lithotomy position and drape with sterile towels as in other operative cases. Cusco's speculum is gently inserted and cervical os visualized. Rarely we may have to hold the cervix with the volsellum.
f. **Cleaning cervical mucus:** The cervix and the vaginal vaults are cleaned of cervical mucus and vaginal secretions using tissue culture media and sterile gauze. Sterile gauze is left at the os for two minutes. It will stick to the mucus plug and pull it out very effectively. We have used warm normal saline to clean the cervix in over 10000 embryo transfers with no compromise in the internationally accepted pregnancy rate.
g. **Ultrasound to visualize cervical canal and uterine cavity:** Inspection of the cervical canal by ultrasound with special emphasis on the cervical uterine angulations and abnormal curvatures.



Ultra-sound guided visualisation of cervical canal & uterine cavity by inner catheter during mock ET

h. Insertion of outer sheath: Insert the outer sheath of the catheter in the cervical canal and stop just above the internal os. If we go further we can damage the endometrium, as the outer sheath is firm and can avulse the endometrial lining.

In case of difficulty in traversing the canal:
If the outer sheath is introduced beyond internal os it may disrupt the endometrium as it is firm in nature. The stimulus of the outer sheath of ET catheter passing through the internal cervical canal and cavity may also initiate uterine contractions.

Gentle uterine sounding may be carried out and catheter outer sheath be inserted till internal os.

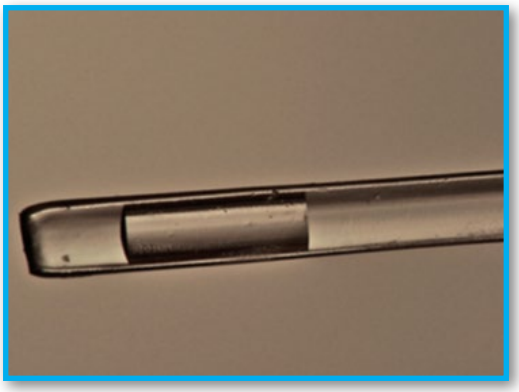
If because of adhesions one cannot negotiate the os, cryo-freezing of all the embryos is recommended followed by transfer after dilation and hysteroscopy

vi. Loading of embryos in the inner catheter

Meanwhile the embryologist will firmly fix the preloaded syringe with the inner soft catheter and push it with its contents—G2 (Vitrolife)/Cleavage pre-equilibrated media. Now the transfer plate is taken out of the incubator and all the embryos in transfer drop are collected together using 170 flexipet. ET catheter tip is brought near the embryos and these are loaded with the embryos in a continuous column of medium (~5-8 µl). The media segment containing the embryos should not be more than 10 µl, followed by very small column of air (~3mm) and then ~2.5 µl of culture media.

Tip: It is important to place the embryos close as this will help in loading them in minimal volume of culture media which is important for good outcome after the embryo transfer.

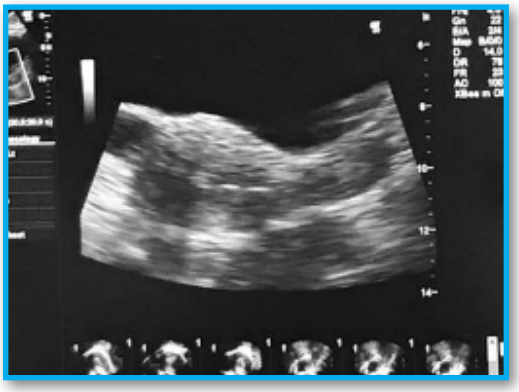
vii. Air bubble technique
Embryos are transferred in culture media bracketed between 2 small air columns. It was suggested that the air bubbles mark the position of the embryos inside the catheter. Air is seen as hyperechoic shadows during ultrasound guided embryo transfer as compared hypoechoic embryo column. This makes the visualization of the embryo column easy as it is seen sandwiched between two hyperechoic areas during embryo transfer. Thus, embryo column is protected against inappropriate placement, and prevents entanglement of the embryos to the mucus plug during embryo transfer.



viii. Deposition of embryo into uterine cavity

The inner catheter containing the embryos at the tip is carried to the transfer room and the inner sheath is inserted in the outer cannula, which is already in the cervical canal. Inner catheter is always carried cupped in the left palm for (right handed) clinicians so that the unnecessary exposure to the air currents and light is avoided. The inner catheter is gently pushed inside and as it transverses the outer sheath and comes to lie around 1 cm from the fundus the plunger is pressed to release the embryos gently. Now gently withdraw the outer and inner sheath. The inner sheath tip is always kept in the outer sheath to avoid sudden temperature changes.

Tip: Once the plunger is pushed it is kept pressed so that there is no negative suction and rotated 360° to release any sticking embryos and mucus plug before withdrawing.



USG guided deposition of embryos into uterine cavity

ix. Prevention of embryo expulsion

According to a recent technique, the use of speculum has been suggested to avoid embryo expulsion after ET. [28]After introducing the ET catheter into the uterine cavity, the screw of the vaginal speculum is loosened so that its two valves press on the portio vaginalis of the cervix, occluding the cervical canal. After one minute, the embryos are pushed in and the catheter is withdrawn slowly. The speculum is kept in place gently pressing on the cervix for about seven more minutes and then removed. The results of this study demonstrated significant improvements in the implantation and pregnancy rates.

x. Inspection for retained embryos:

The catheter is immediately handed over to the embryologist who releases the contact between the syringe and the catheter and the contents of the catheter are emptied on the sterile dish cover. The catheter tip is gently rolled on the lid and inspected for retained embryos, blood, and mucus.

a. **Protocol for retained embryos:** If we have retained embryos they are immediately rinsed in G1 (Vitrolife) / Cleavage media and transferred to fresh well with G2 (Vitrolife) / Cleavage pre-equilibrated media. The embryos are allowed to equilibrate for approximately 1 hr before these are transferred again.

Growing tendency towards transferring less embryos, preferably a single embryo has motivated the ART teams to alter their methodologies as ET has lately been acknowledged as a decisive step in an IVF cycle.

Part - 3

Frequently Asked Questions (FAQs)

INDEX

Part : 3
Frequently Asked Questions (FAQs)

1 What is the role of uterine contractions in Embryo Transfer?

Uterine contractions at the time of ET are associated with a lower pregnancy rate. Initiation of uterine contractions may lead to an immediate or delayed expulsion of the embryos and has been considered a big concern in ART. Generally uterine contractions are due to the tightening and shorting of the uterine muscles.
Prostaglandins present in the uterus play the pivotal role in contraction of smooth muscles of uterus and biophysical changes associated with it.

2 How to avoid uterine contractions?

Administration of vaginal progesterone two days before ET can significantly reduce the frequency of uterine contractions (could be effective for restoring utero-relaxation at the time of ET) and improve embryo implantation.

3 How cervical mucus affect the rate of implantation?

Cervical mucus by covering the catheter tip, may initiate the dragging of embryos. It can be one of the sources of bacterial contamination of uterine cavity. Potential concerns of presence of cervical mucus at the time of ET may decrease the transfer efficiency and increase the embryo expulsion. There are studies which contradict the removal of cervical mucus during embryo transfer and its impact on the rate of pregnancy. Some reported no positive effect on the pregnancy rate while other supports. Cervical mucus culture tested positive in more than 50% of patients at the catheter tip. Cleaning and cervical mucus aspiration can decrease infection rate with Uroplasma, Streptococcus B, D, Staphylococcus, E. coli, Mycoplasma and increase implantation rate.

4 What are main causes of cervical mucus?

Cervical mucus is a fluid secreted by the cervix, the production of which is stimulated by the hormone estrogen and it's a biological indicator of fertility window. Throughout menstrual cycle, the amount and quality of cervical mucus that is produced will fluctuate. At the time of ovulation, estrogen levels begin to surge, which causes cervix to secrete more cervical mucus that is of a so-called "fertile quality". After ovulation, the quantity of cervical mucus begins to decline and become thicker in consistency. The fertile-quality cervical mucus, also known as Egg White Cervical Mucus (EWCM), is clear, stretchy and the perfect protective medium for sperm in terms of texture and pH.

5 What is "dragging of embryos"?

Embryo dragging and the amount of cervical mucus present within the cervical canal throughout embryo transfer are directly proportional to each other. The possibility of embryo dragging will increase in presence of excess of mucus. At the time of embryo transfer, mucus might also block the passage of embryos through the tip of the catheter and may cause the difficulty in injecting the embryos. Cervical mucus drag the embryos back from the site of placement because the embryos are probable to stick to the side of the catheter during catheter withdrawal. Embryos can also get embedded within the cervical mucus.

6 What is the role of Mock ET?

Mock ET plays an important role to improve the pregnancy rate significantly. With mock ET, we can calculate the length of the uterine cavity and evaluate its direction and the degree of cervico-uterine angulations.

Mock ET can be performed the month before your actual IVF cycle, usually when the reproductive system is being quieted down with lupride (The most common time). Or at the time of oocyte retrieval or 3 to 5 days before ET.

No deleterious effect of mock ET on the endometrium has been seen. It is also useful for selecting the most suitable kind of catheter. Presence of polyps or fibroids, pinpoint external os and stenosed cervix from previous surgery can also be discovered with mock ET.

7 What is the importance of catheters in Embryo Transfer?

- The ideal ET catheter should be safe, user friendly and soft enough to avoid any trauma to the endo-cervical canal or endometrial cavity.
- It should be easily visible under USG.
- Catheter should be pliable enough to negotiate through the cervical canal into the endometrial cavity.
- Additionally, its tip should be smooth and non-traumatic to the lining of endometrium.
- Ideal catheters are of co-axial variety. The outer sheath should also be malleable and inserted till internal os very gently.

8 What is the difference between Blind ET and Ultrasound guided ET?

It is called Blind ET when clinician feels the resistance of internal os and then advances the catheter by 3- 4 cm and position the embryos and Ultrasound guided ET involves the deposition of embryos into the uterine cavity at a fixed distance from the fundus under ultrasound vision.

9 What should be the ideal volume of media for loading of embryos during Embryo Transfer?

A continuous column (~5-8 µl) of culture media followed by ~3 mm column of air is recommended during embryo transfer. Column of air allow the easier visualization via ultrasound.

10 What should be the pressure on the plunger during injection or withdrawal of inner catheter?

After the visualization of catheter tip through ultrasound in the mid or lower mid portion of the uterus, the embryologist should press the plunger slowly and steady to expel the embryos. Slow pressure is required to protect the embryos from the pressure gradient change.

11 Why inner catheter should be pulled out slowly after injecting of embryos?

Post embryo transfer, the inner catheter should be withdrawn slowly from the uterus to avoid creating negative pressure or a "plunger effect". The outer sheath and inner catheter should retract completely and together to avoid these "negative effects".

12 What should be the ideal time from loading of the embryos till transfer?

The time interval from loading the embryos in the catheter to depositing them in the uterine cavity should be kept to a minimum in order to prevent prolonged exposure of the embryos to ambient temperature, light, or other factors. A long time of more than 60 seconds or 120 seconds has been shown to lower the pregnancy and implantation rates. On the other hand, another study showed no adverse effect of the duration of the procedure on the results, even with transfers lasting up to 7.5 minutes.

13 How to avoid Ectopic Pregnancy?

The distance from the fundus to the tip of the ET catheter was studied in relation to the ectopic rate. The authors reported a decrease in the ectopic rate associated with an increased distance between the fundus and the tip of the catheter. The mid-fundal technique resulted in a lower percentage of ectopic pregnancy and did not negatively affect the pregnancy rate.

14 What is Difficult ET?

ET is considered difficult when clinician find difficult to pass ET catheter through cervical canal and internal os due to tight cervix or lack of alignment between catheter and utero-cervical angle.

15 What is the importance of air gap in Air Bubble Technique?

Air bubbles mark the position of the embryos inside the catheter. Air is seen as hyperechoic shadows during ultrasound guided embryo transfer as compared hypoechoic embryo column. It makes the visualization of the embryo column easy and embryo column is protected against inappropriate placement.

16 How embryos are graded?

The embryo quality can be assessed by morphology and its metabolic process.
Mostly scoring systems are based on several morphological parameters such as.

a) Cleavage stage
b) Embryonic fragmentation
c) Blastomere uniformity and number

The newer techniques, such as time lapse, PrimoVision, and Miri® include multilevel digital recording of embryo images and software programs that allow detailed interpretation of the embryo pictures and help in selection.
Micro methods such as Embryos' respiratory rate, Glucose consumption, Nitric oxide levels and amino acid turnover pace are used for assessing the metabolism of embryos in order to improve the selection of embryos with the best developmental potential.

17 What should be the ideal thickness of endometrium for Embryo Transfer?

Adequate endometrial development is required for pregnancy to occur as pregnancy rates were found to be higher when the endometrium reached at least 9 mm thickness with a triple line pattern and other prognostic factors, such as embryo quality and age, are taken into consideration. A markedly thick endometrium also deters implantation. Likewise, the endometrial volume, measured with 3D ultrasound, of less than 2.5 ml on the day of transfer showed poor probability of implantation.

18 What is the Maximum Implantation Potential (MIP) point?

Embryo implants in the specific area in the posterior wall of the uterus where the endometrium is most receptive. This certain point of area is called as Maximum Implantation Potential (MIP) point. This MIP point is identified as intersection of two imaginary lines originating from each fallopian tube. This intersection is referred as MIP / midpoint which can only be visualized by 3D ultrasound and varies from patient to patient upon shape of the uterus.

19 Refrences

1. Zhu L1, Che HS, Xiao L, Li YP. Uterine peristalsis before embryo transfer affects the chance of clinical pregnancy in fresh and frozen-thawed embryo transfer cycles. *Hum Reprod*. 2014 Jun; 29(6):1238-43.
2. Fanchin R, Ayoubi JM, Righini C, Olivennes F, Schönauer LM, Frydman R. Uterine contractility decreases at the time of blastocyst transfers. *Hum Reprod.* 2001; 16:1115–9.
3. Visschers BA, Bots RS, Peeters MF, Mol BW, van Dessel JH. Removal of cervical mucus: E ect on pregnancy rates in IVF/ICSI. *Reprod Biomed Online*. 2007; 15: 310–5.
4. Eskandar MA, Abou-setta AM, El-Amin M, Almushait MA, Sobande AA. Removal of cervical mucus prior to embryo transfer improves pregnancy rates in women undergoing assisted reproduction. *Reprod Biomed Online.* 2007; 14: 308–13.
5. Egbase PE, Al-Sharhan M, Al-Mutawa M, Udo EE, Grudzinskas JG. Incidence of microbial growth from the tip of embryo transfer catheter after embryo transfer in relation to clinical pregnancy rate following in vitro fertilization and embryo transfer. *Hum Reprod.* 1996; 11:1687.
6. Fanchin R, Harmas A, Benaoudia F, Lundkvist U, Olivennes F, Frydman R. Microbial flora of the cervix assessed at the time of embryo transfer adversely affects invitro fertilization outcome. *Fertil Steril.* 1998; 70:866.
7. Moragianni VA, Cohen JD, Smith SE, Schinfeld JS, Somkuti SG, Lee A, Barmat LI. E ect of macroscopic or microscopic blood and mucus on the success rates of embryo transfers. *Fertil Steril.* 2010; 93(2): 570–3.
8. Derks RS, Farquhar C, Mol BW, Buckingham K, Heineman MJ. Techniques for preparation prior to embryo transfer. *Cochrane Database Syst Rev*. 2009; 4: CD007682.
9. Poindexter AN 3rd, Thompson DJ, Gibbons WE, et al. Residual embryos in failed embryo transfer. *Fertil Steril.* 1986; 46:262–7.
10. Henne MB, Milki AA. Uterine position at real embryo transfer compared with mock embryo transfer. *Hum Reprod.* 2004; 19(3):570–2.
11. Sallam HN, Agameya AF, Rahman AF, Ezzeldin F, Sallam AN. Ultrasound measurement of the uterocervical angle before embryo transfer: a prospective con- trolled study. *Hum Reprod.* 2002; 17(7):1767–72.
12. Brown J, Buckingham K, Abou-Setta AM, Buckett W. Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women. *Cochrane Database Syst Rev.* 2010; 1:CD006107.
13. Buckett WM. A review and meta-analysis of prospective trials comparing different catheters used for embryo transfer. *Fertil Steril.* 2006; 85(3):728–34.
14. Abou-Setta A M, Al-Inany HG, Mansour RT, Serour GI, Aboulghar MA. Soft versus firm embryo transfer catheters for assisted reproduction: a systematic review and meta-analysis. *Hum Reprod.* 2005; 20(11):3114–21. 2.
15. Mansour R, Aboulghar M, Serour G. Dummy embryo transfer: a technique that minimizes the problems of embryo transfer and improves the pregnancy rate in human in vitro fertilization. *Fertil Steril.* 1990; 54:678–81.
16. Kovacs GT. What factors are important for successful embryo transfer after in vitro fertilization? *Hum Reprod.* 1999; 14:590.
17. Angelini A, Brusco GF, Barnocchi N, El-Danasouri I, Pacchiarotti A, Selman HA. Impact of physician performing embryo transfer on pregnancy rates in an assisted reproductive program. *J Assist Reprod Genet*. 2006; 23:329–32.
18. Ciray HN, Tosun S, Hacifazlioglu O, Mesut A, Bahceci M. Prolonged duration of transfer does not affect outcome in cycles with good embryo quality. *Fertil Steril*. 2007; 87(5): 1218–21.
19. Bar-Hava I, Kerner R, Yoeli R, Ashknazi J, Shalev Y, Orvieto R. Immediate ambulation after embryo transfer: a prospective study. *Fertil Steril.* 2005; 83:594.
20. Tremellen KP, Valbuena D, Landeras J, et al. The effect of intercourse on pregnancy rates during assisted human reproduction. *Hum Reprod.* 2000; 15:2653–8.
21. Baruffi R, Mauri AL, Petersen CG, Felipe V, Franco JG Jr. Effects of vaginal progesterone administration staring on the day of oocytes retrieval on pregnancy rates. *J Assist Reprod Genent.* 2003; 20:517.
22. Moon HS, Park SH, Lee JO, Kim KS, Joo BS. Treatment with piroxicam before embryo transfer increases the pregnancy rate after in vitro fertilization and embryo transfer. *Fertil Steril.* 2004; 8:816.
23. Cohen J, Mayaux MJ, Guihard-Moscato ML, Schwartz D. In-vitro fertilization and embryo transfer: A collaborative study of 1163 pregnancies on the incidence and risk factors of ectopic pregnancies. *Hum Reprod* 1986; 1(4): 255–8.
24. Refaat B, Dalton E, Ledger WL. Ectopic pregnancy secondary to in vitro fertilization–embryo transfer: Pathogenic mechanisms and management strategies. *Reprod Biol Endocrinol* 2015; 13(1): 30.
25. Nazari A, Askari HA, Check JH, O'Shaughnessy A. Embryo transfer technique as a cause of ectopic pregnancy in in vitro fertilization. *Fertil Steril* 1993; 60(5): 919–21.
26. Lesny P, Killick SR, Tetlow RL, Robinson J, Maguiness SD. Uterine junctional zone contractions during assisted reproduction cycles. *Hum Reprod* Update 1998; 4(4): 440–5.
27. Mansour R, Tawab N, Kamal O, El-Faissal Y, Serour A, Aboulghar M, Serour G. Intrauterine injection of human chorionic gonadotropin before embryo transfer significantly improves the implantation and pregnancy rates in in vitro fertilization/intracytoplasmic sperm injection: A prospective randomized study. *Fertil Steril* 2011; 96(6): 1370–1374.
28. Mansour R. Minimizing embryo expulsion after embryo transfer: A randomized controlled study. *Hum Reprod.* 2005; 20(1): 170–4.

Part - 4

Embryo Transfer Catheters from different OEMS

INDEX

Part : 4
Embryo Transfer Catheters from different OEMS

Comparison of Embryo Transfer catheters from different OEMs

S. No.	OEM	Type	Specifications	Key features
1	Wallace	(a) Wallace® Classic	**Inner catheter inner diameter** – 0.76 mm **Inner catheter outer diameter** – 1.52 mm **Outer sheath outer diameter** – 2.3 mm **Volume of the catheter not including hub** – (18 cm catheter) – 0.081 ml (81 µl) **Volume of the catheter not including hub** – (23 cm catheter) – 0.104 ml (104 µl) **Volume per cm length of catheter** – 0.0045 ml (4.5 µl) **Suggested loading volume** – 0.5 to 1 cm = 2.25 to 4.5 µl **Stylet outer diameter** – 1.52 mm **Stylet protrusion from outer sheath** – 2.0 mm	**Soft material** and **smooth tip** minimizes trauma and maximizes success rates. **Formable Outer Sheath** to suit different patient anatomies. **Centimeters markings to show outer sheath depth and inner lumen protrusion** for confidence of placement within the uterus. Trial transfer catheters allow for **confident positioning** of the outer sheath before introducing the embryo loaded inner. Catheters are available in **two sizes** i.e. 18 cm and 23 cm.

S. No.	OEM	Type	Specifications	Key features
1	Wallace	(b) Wallace® Sure-Pro®	**Inner catheter inner diameter** – 0.76 mm **Inner catheter outer diameter** – 1.52 mm **Outer sheath outer diameter** – 2.5 mm **Volume of the catheter not including hub** – (18 cm catheter) – 0.104 ml (104 µl) **Volume per cm length of catheter** – 0.0045 ml (4.5 µl) **Suggested loading volume** – 0.5 to 1 cm = 2.25 to 4.5 µl **Stylet outer diameter** – 1.52 mm **Stylet protrusion from outer sheath** – 2.7 mm	**Supported inner catheter** for increased control during handling and insertion. **Pre-formed curve** on outer sheath to help navigate the cervical canal. **Adjustable silicone marker** for **depth guidance and tip orientation.** Available with or without a **Soft Obturator** and **Firm Stylet** to suit various techniques and patient anatomies. The **Soft Obturator** can be used in an elective 2 stage transfer to allow navigation of the outer sheath through the cervical canal. Once in position the **Obturator is removed** and the **embryo loaded inner catheter inserted through the outer sheath** into the uterus. The Stylet is used in the same way but offers a **firmer** solution for more **difficult cases.** **Supplied in a procedural tray** to maintain sterility whilst handling. Sure-Pro Embryo Replacement Catheter is available in 23 cm.

S. No.	OEM	Type	Specifications	Key features
1	**Wallace**	**(c) Wallace® Sure View**	**Inner catheter inner diameter** – 0.76 mm **Inner catheter outer diameter** – 1.52 mm **Outer sheath outer diameter** – 2.3 mm **Volume of the catheter not including hub** (18 cm catheter) – 0.081 ml (81 µl) **Volume of the catheter not including hub** (23 cm catheter) – 0.104 ml (104 µl) **Volume per cm length of catheter** – 0.0045 ml (4.5 µl) **Suggested loading volume** – 0.5 to 1 cm = 2.25 to 4.5 µl **Stylet outer diameter** – 1.52 mm **Stylet protrusion from outer sheath** – 2.0 mm	**Visible** under ultrasound from **hub to tip.** More **accuracy** and **confidence** when positioning catheter tip within uterus for embryo replacement. Combines the benefits of the Classic range with the **Sure View®** patented technology. Compatible with the Wallace Malleable Stylet for difficult transfers. Sure View® Embryo Replacement Catheter and Sure View® are **available in two sizes** i.e. 18 cm and 23 cm.

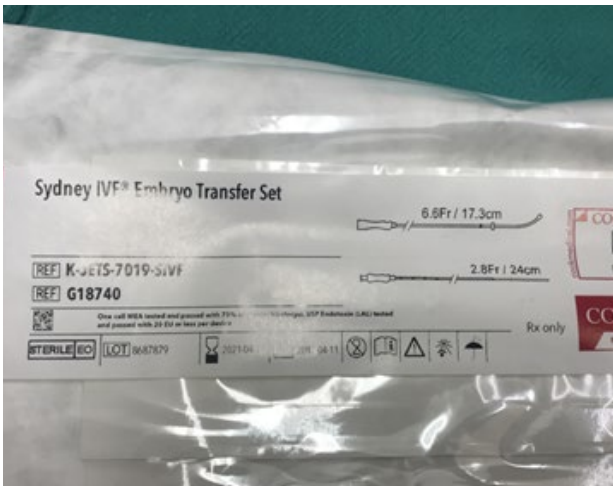
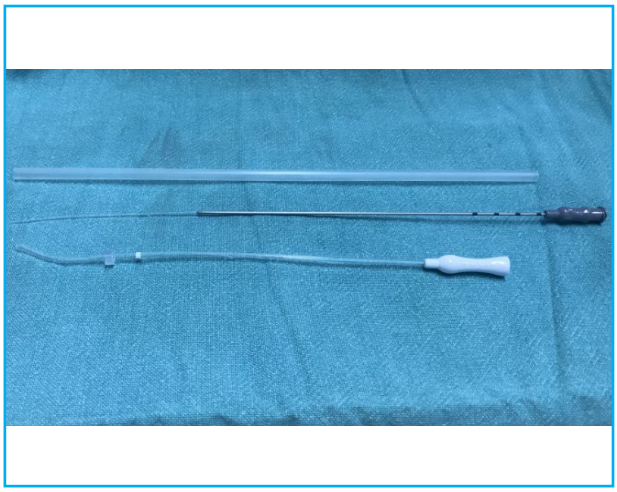
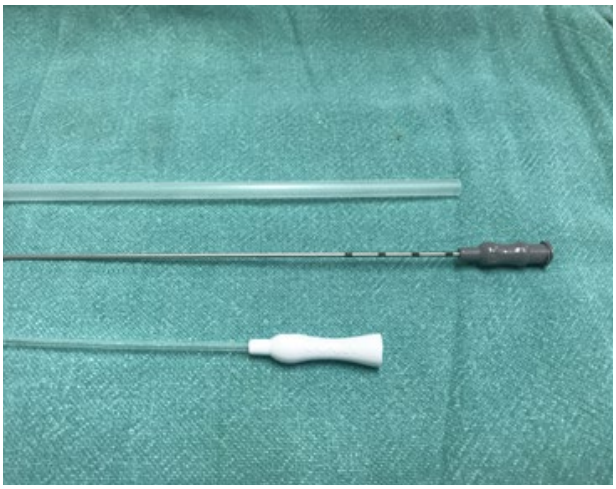
S. No.	OEM	Type	Specifications	Key features
1	**Wallace**	**(d) Wallace® Sure-Pro Ultra® (PEB623)**	**Inner catheter inner diameter** – 0.76 mm **Inner catheter outer diameter** – 1.52 mm **Outer sheath outer diameter** – 2.5 mm **Volume of the catheter not including hub** – (18 cm catheter) – 0.104 ml (104 µl) **Volume per cm length of catheter** – 0.0045 ml (4.5 µl) **Suggested loading volume** – 0.5 to 1 cm = 2.25 to 4.5 µl **Stylet outer diameter** – 1.52 mm **Stylet protrusion from outer sheath** – 2.7 mm	**Sure View®** patented air bubble technology allows for the whole catheter length to be viewed under ultrasound. Supported inner catheter improves **control of handling** and insertion. Retains the Soft Hand crafted tip of the world recognized **Wallace® Classic** catheter. **Formable outer sheath** allowing for accentuation or smoothing of the pre-formed curve. **Pre-formed curve** on outer sheath to help navigate the cervical canal. **Adjustable silicone marker for depth guidance and tip orientation.** **Available with a soft obturator** and **firm stylet** to suit various techniques and patient anatomies.

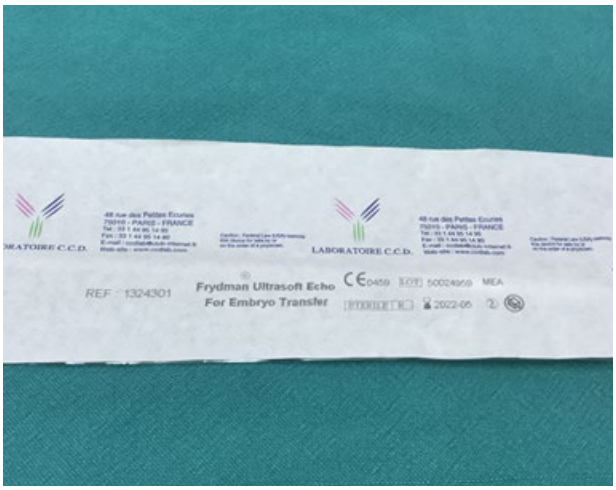
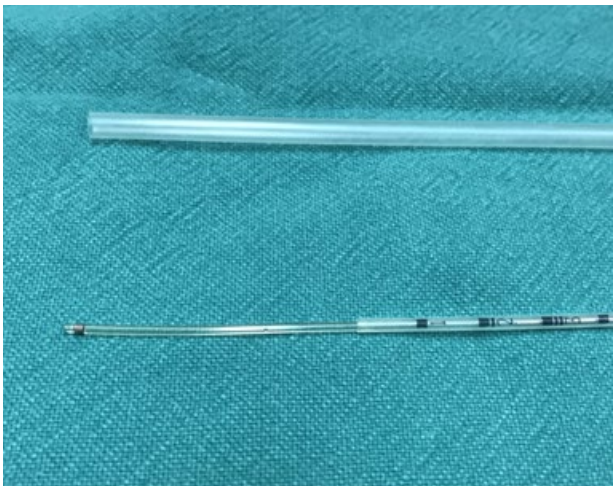
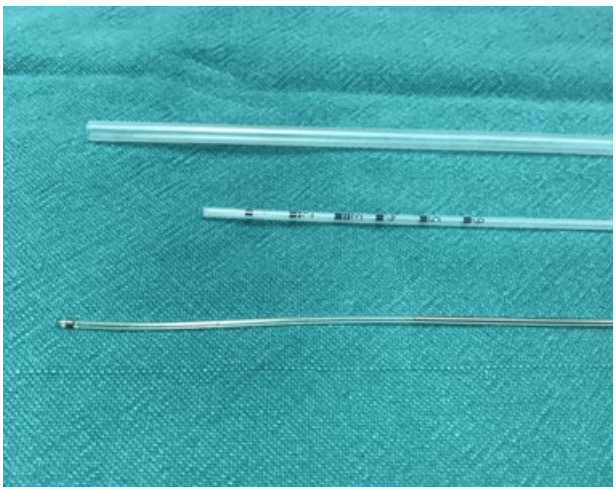
S. No.	OEM	Type	Specifications	Key features
2	**COOK Medical**	**Sydney IVF Embryo Transfer Catheter Sets**	**i) Type** – Catheters Packed Assembled **Product No.** – G20683 **Guide Catheter (Fr)** – 6.6 **Guide Catheter Length (cm)** – 16.7 **Transfer Catheter (Fr)** – 2.8 **Transfer Catheter Length (cm)** – 23 **Guide Catheter Hub Style** – Silicon **ii) Type** – Catheters Packed Separately **Product No.** – G18740 **Guide Catheter (Fr)** – 6.6 **Guide Catheter Length (cm)** – 17.3 **Transfer Catheter (Fr)** – 2.8 **Transfer Catheter Length (cm)** – 24 **Guide Catheter Hub Style** – Polycarbonate **Others** – Malleable obturator is also available to fit the catheter	Catheter is **used for** the **atraumatic transfer** of embryos into the uterine cavity. **Pre-curved guiding** catheter facilitates catheter insertion. **Atraumatic bulb tip** eases passage through cervix. **Soft, flexible transfer catheter minimizes endometrial trauma.** **Microvol™** technology reduces the **volume of medium** required to transfer embryos. Cervical stop comes set at 4 cm with an additional stop at 5 cm.

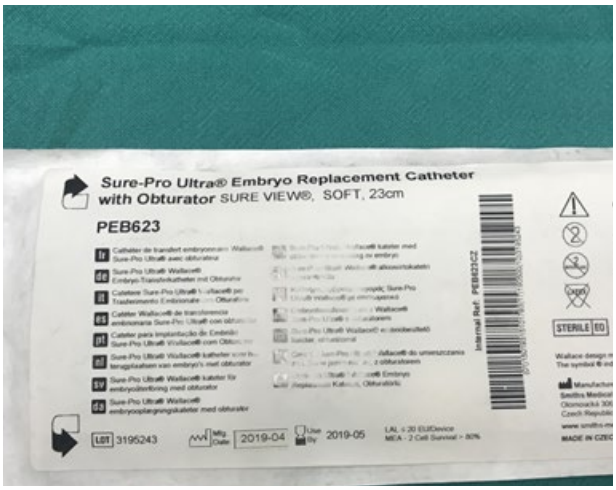
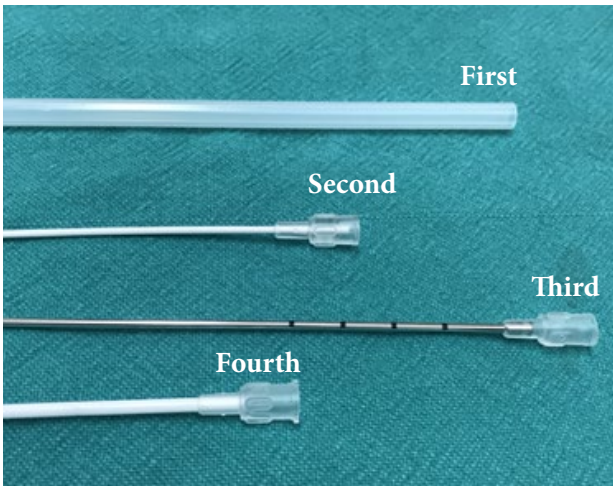
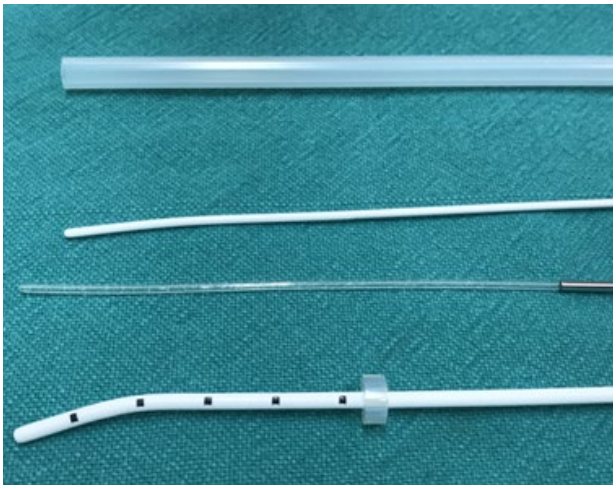
S. No.	OEM	Type	Specifications	Key features
3	**CCD Laboratoire**	**Frydman® Ultrasoft Echo** **Frydman® Ultrasoft** **Frydman® Full Echo Pro** **Frydman® Classic 4.5**	**Product Code –** **1324201 :** Frydman® Ultrasoft **1324301 :** Frydman® Ultrasoft Echo **i) OUTER SHEATH** **Usable length** – 14.5 cm **Length of flexible tip** – N/A **Internal volume** – N/A **Inner diameter** – N/A **Outer diameter** – 2.20 mm **Markings** – 6 insertion guide marks on distal segment **Components** – Polypropylene **Color code** – White base **ii) STYLET** **Usable length** – 17.5 cm **Length of flexible tip** – N/A **Internal volume** – N/A **Inner diameter** – N/A **Outer diameter** – 1.55 mm **Markings** – N/A **Components** – Polyethylene coated steel **Color code** – Green base **iii) TRANSFER CATHETER** **Usable length** – 21.5 cm **Length of flexible tip** – 4.5 cm **Internal volume** – 0.20 ml **Inner diameter** – 1.55 mm **Outer diameter** – 4 insertion guide marks near the base markings **Components** – Polyurethane **Color code** – White base	**The devices include:** • An **outer sheath in polypropylene** with 6 insertion guide-marks. • A **transfer catheter in ultra soft polyurethane** in its distal section and rigidified in its proximal section by an internal sheath, to help its handling. The **echogenic model** of this catheter **has** a **beveled ring at its tip in brushed stainless steel visible on ultrasound images.** When placed in the outer sheath, the transfer catheter sticks out by 4.5 cm from the distal extremity of the outer sheath. The length of the catheter inside the uterus can be calculated from the insertion guide-marks near the base. **A stylet** is available separately. The **trial transfer catheter** presents similar features to the real transfer catheters Frydman® Ultrasoft Echo, but its extremity is closed and the metal echogenic marker is embedded in the catheter tip. Its base is green.

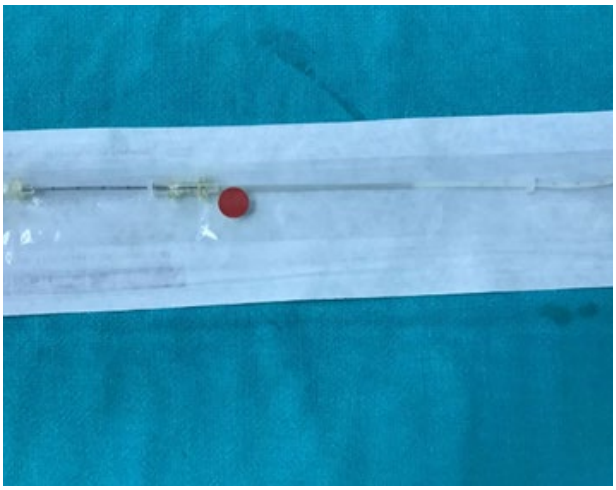
S. No.	OEM	Type	Specifications	Key features
4	**Labotect**	**Labotect Embryo Transfer Catheter set**	**Product No**. – 13365 **Length** – 150 mm **Product No.** – 13366 **Length** – 190 mm **Product No.** – 13369 **Length** – 230 mm **Packaging** – Hard blister, inner catheter and guiding cannula single packed. **Product No.** – 14690 (single packed) **Length** – 190 mm	The **Luer connection** at the proximal end of the guiding cannula **permits trouble-free insertion of the inner catheter.** The **penetration depth** and the **direction can be set at the guiding cannula using a slide ring.** **Atraumatic owing to the curved guiding cannula with a ball end,** allowing the set to be used reliably even with difficult anatomic conditions. **Metal reinforced inner catheter shaft allows simple, safe handling.** **Three different lengths** permit optimal adaption to different anatomies. **Disposable product, double sterile packed.**

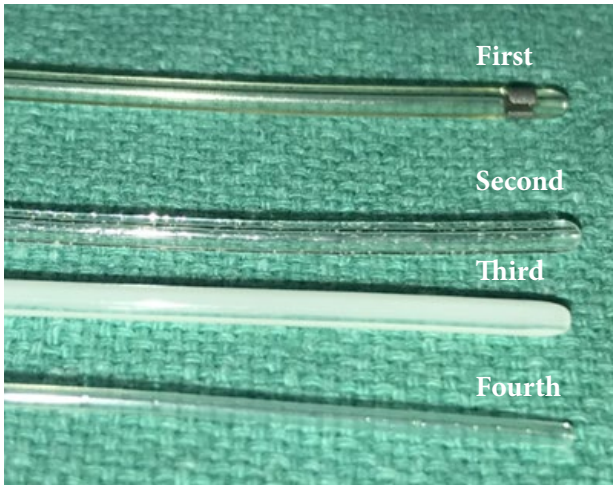
Table 2: Embryo Transfer Catheters from different OEMs

S.No	OEM	FIGURE	LEGEND
1	COOK		**Sydney IVF Embryo Transfer Set** (K-JETS-7019-SIVF).
			**Figure shows:** • **Topmost:** Outer covering of Transfer Catheter. • **Middle:** Transfer Catheter with **Echogenic tip.** • **Lowermost:** Outer sheath with **adjustable stopper.**
			**Centimeter depth marking** near the Silicon hub of transfer catheter to represent the **inner catheter tip protrusions from the outer sheath.** Outer sheath with **standard silicone hub.**

S.No	OEM	FIGURE	LEGEND
2	CCD Laboratoire		**CCD Laboratoire Frydman Ultrasoft Echo Embryo Transfer Set.**
			**Figure shows:** • **Topmost:** Outer covering of Transfer Catheter. • **Below:** Transfer Catheter. The **Echogenic model** of this catheter has a **beveled ring at its tip in brushed stainless steel visible on ultrasound images.**
			**Figure shows:** • **Topmost:** Outer covering of Transfer Catheter. • **Middle:** Outer Sheath in polypropylene with 6 insertion guide-marks. • **Below:** Transfer Catheter.

S.No	OEM	FIGURE	LEGEND
3	WALLACE		**Sure- Pro Ultra® Embryo Replacement Catheter with Obturator.**
			**Figure shows:** • **First: Outer cover** of Transfer Catheter. • **Second: Stylet** with **silicone hub.** • **Third: Transfer catheter** with **silicone hub** and **4 black centimeter depth** markings to represent the inner catheter tip protrusion from the outer sheath. • **Fourth: Outer sheath** with **silicone hub.**
			**Supported inner catheter** with **unique Echogenic** properties which allows full visibility under ultrasound. **Pre-formed curve** on outer sheath to help navigate the cervical canal with **adjustable silicone marker** for depth guidance and tip orientation.

S.No	OEM	FIGURE	LEGEND
4	Labotect		**Labotect Embryo Transfer Catheter Set.**
			**Handle** with **luer lock** for a more secure fitting to syringes. **Markings to indicate depth.**

S.No	OEM	FIGURE	LEGEND
5			**Figure shows:** **First: CCD Frydman® Ultra-soft catheter** (Ref no.-1324301) in 2 pieces, with Echogenic ring for better of its positioning. **Second:** Transparent **Wallace Sure-Pro Ultra** (PEB 623) catheter with **Patented (Air Bubble) Sure View technology** which allows full visibility under ultrasound. **Third: CCD Frydman® Full Echo Pro catheter** which allows full visibility under ultrasound. The lines are made up of inox mandrel with Barium Sulphate (BaSO4). **Fourth:** Transparent **COOK Sydney IVF** (K-JETS-7019-SIVF) embryo transfer catheter.

Part - 5

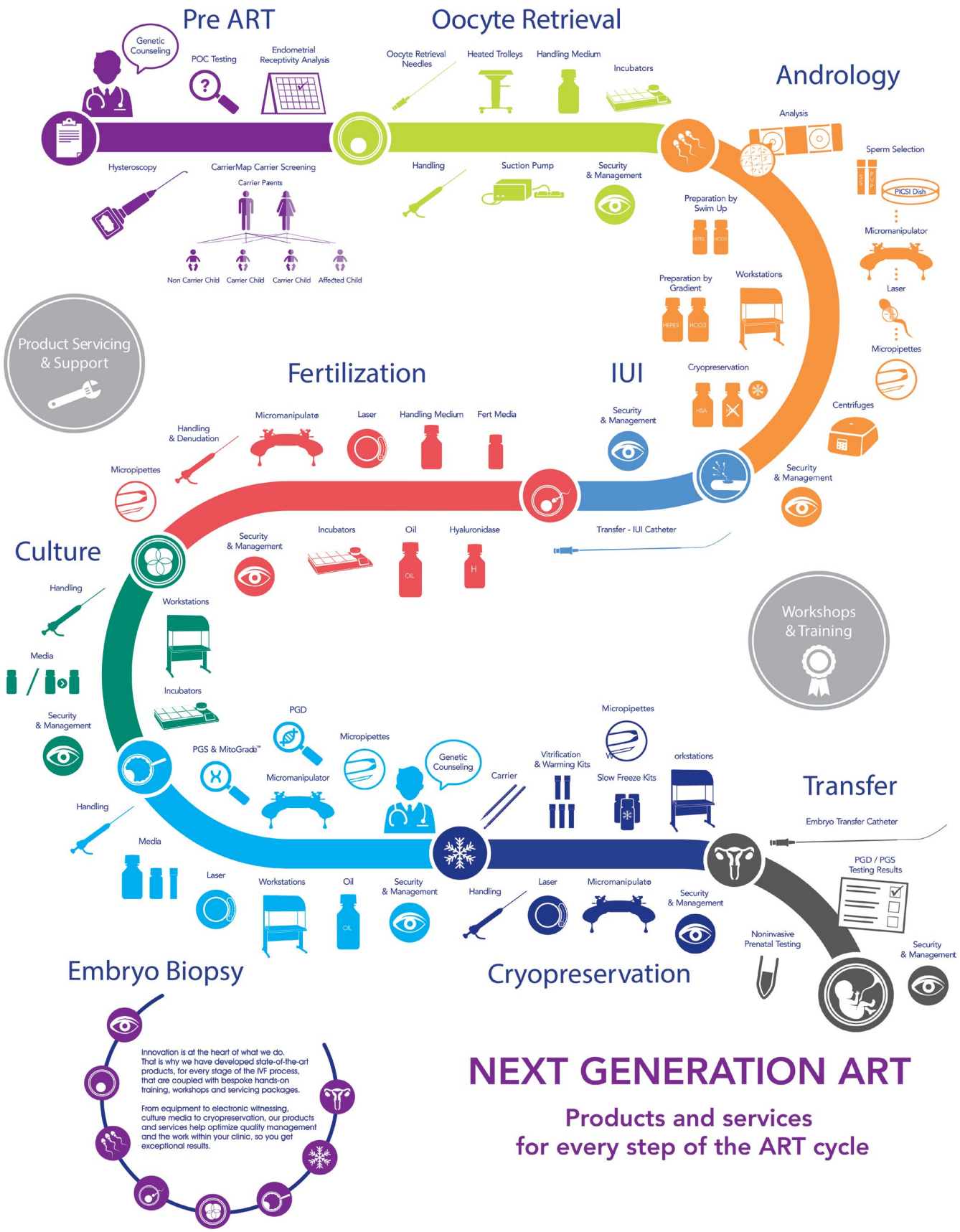
Original Equipment Manufacturers (OEM) and Vendor details

Table - OEM & Vendor Related Contact Information for OPU needles

S. No.	Original Equipment Manufacturer (OEM)	India Distributer	Device Brand	Price per Device	Contact Person	Phone	Email
1	**CooperSurgicals,Origio** o/s, knardrupuejz 2, DK-2760. Malov, Denmark	Shivani Scientific India Pvt. Ltd.	Wallace	Not disclosed	Mr. Ashish Patole	+91 9324492112	sales@shivaniscientific.com
2	**Labotect Labor Techniks**, Göttingen, Germany	Vision Diagnostics Pvt. Ltd.	Labotect	Not disclosed	Mr. Punit Khatnani	+91 9910188771	punit@vision-groups.com
3	**CryoBio System** Groupe I.M.V Technologies France	CryoBio System India	CCD Laboratoire	Not disclosed	Mr. Jitender Kumar	+919650602424	jitender@cryobio-systemindia.com
4	**COOK Medical Inc.** P.O Box 4195, Bloomington, In 474024195, USA	Intermedics	COOK	Not disclosed	Mr. Gopal	+919212798185	projects@intermedics.in

Notes

Notes



ORIGIO India Private Limited
C - 401, Delphi, Hiranandani Business Park, Powai,
Mumbai - 400 076, Maharashtra, India
Board Line No. : +91 22-49280000 I Fax No. +91 22-49280010

CooperSurgical Companies Product Portfolio

Pre ART

- CarrierMap ™
- Genetic Counseling
- Endosee ® (hysteroscopy)
- ERGrade ™ Endometrial Receptivity Analysis
- POC Testing

Oocyte Retrieval

- Oocyte Retrieval Needles
- Wallace ® Single Lumen Oocyte Recovery Needle*
- Wallace ® Single Lumen Oocyte Recovery Sets
- Wallace ® Dual Lumen Oocyte Recovery Sets*
- ORIGIO Stiff Oocyte Retrieval Needles*
- ORIGIO Regular Wall Oocyte Retrieval Needles*
- ORIGIO Thin Wall Oocyte Retrieval Needles*
- ORIGIO Double Lumen Oocyte Retrieval Needles*
- Suction Pump
- ORIGIO Suction Pump*
- Handling Devices
- The Stripper ® (Standard / BP / CC / PGD)
- RI EZ-Range (RI EZ-Grip ®, RI EZ-Strip ®, RI EZ-Squeeze ™, RI EZ-Tip ®)
- IVF Pasteur Pipets
- The Stripper Tips (Individual or Multi Pack)
- Media
- Quinn's Advantage Medium with HEPES
- Flushing Media
- SynVitro Flush
- Heated Trolley
- K-Systems Trolley with Warmed Table Top*
- K-Systems Warming Plates T45/T47*
- Incubators
- K-Systems G210 InviCell*
- K-Systems G185*
- ORIGIO ® / PLANER Benchtop Incubator BT37
- Security & Management
- RI Witness ™

Andrology

- Analysis
- HBA ® Assay
- Preparation by Swim Up
- ORIGIO Sperm Preparation Media
- Quinn's ™ Sperm Washing Medium
- Preparation by Gradient
- PureCeption ™
- Quinn's ™ Sperm Washing Medium
- SupraSperm ®
- ORIGIO Sperm Preparation Media
- Centrifuges
- Midi/Maxi
- Sperm Selection
- SpermSlow ™
- PICSI ® Dish
- PVP (PVP Medium, PVP Clinical Grade, PVP 7% Solution)
- ORIGIO, TPC and RI Micropipettes
- Cryopreservation
- CryoSperm ™
- Sperm Freezing Medium
- Quinn's Advantage ™ Sperm Freezing Medium
- Micromanipulator
- Integra 3 ™ Micromanipulator
- Laser
- Saturn 5 ™ Laser System
- Workstations – Class I
- K-Systems 100 Series (L124 / L124 ICSI/ L126 MP)*
- ORIGIO Fortuna
- ORIGIO Titan
- Workstations – Class II
- K-Systems L234 CellTouch*
- K-Systems G603 Work Chamber*
- ORIGIO Mars
- Supporting Products
- Warming Blocks
- Glass Hoods
- Gas Line Filters
- Security & Management
- RI Witness ™

IUI

- Handling Devices
- Wallace ® Intrauterine Insemination Catheter
- ORIGIO IUI Cathether*
- IVF Pasteur Pipets
- Security & Management
- RI Witness ™

Fertilization

- Handling and Denudation Devices
- The Stripper ® (Standard / BP / CC / PGD)
- RI EZ-Range (RI EZ-Grip, RI EZ-Strip, RI EZ-Squeeze, RI EZ-Tip)
- IVF Pasteur Pipets
- The Stripper Tips (Individual or Multi Pack)
- Media
- ORIGIO ICSI Cumulase ®
- SAGE Hyaluronidase
- ORIGIO SynVitro ® Hyadase
- Quinn's Advantage ™ Fertilization (HTF) Medium
- Quinn's Advantage ™ Protein Plus Fertilization (HTF) Medium
- ORIGIO Sequential Fert ™
- Oil
- ORIGIO Liquid Paraffin
- SAGE Oil for Tissue Culture
- Incubators
- K-Systems G210 InviCell*
- K-Systems G185*
- ORIGIO ® / PLANER Benchtop Incubator BT37
- Workstations – Class I
- K-Systems 100 Series (L124 / L124 ICSI / L126 MP)*
- ORIGIO Fortuna
- ORIGIO Titan
- Workstations – Class II
- K-Systems L234 CellTouch*
- K-Systems G603 Work Chamber*
- ORIGIO Mars
- Micropipettes
- ORIGIO Holding and Injection Pipettes
- TPC Holding and Injection Pipettes
- RI Holding and Injection Pipettes
- Wallace ® Holding and Injection Pipettes
- Micromanipulator
- Integra 3 ™ Micromanipulator
- Laser
- Saturn 5 ™ Laser System
- Security & Management
- RI Witness ™

*Not available in the USA

Culture

- Media
- Quinn's Advantage ™ Cleavage Medium
- Quinn's Advantage ™ Blastocyst Medium
- Quinn's Advantage ™ Protein Plus Cleavage Medium
- Quinn's Advantage ™ Protein Plus Blastocyst Medium
- ORIGIO Sequential Cleav ™
- ORIGIO Sequential Blast ™
- EmbryoGen ® & BlastGen ™
- SAGE 1-Step ™
- Oil
- ORIGIO Liquid Paraffin
- SAGE Oil for Tissue Culture
- Handling Devices
- The Stripper ® (Standard / BP / CC / PGD)
- RI EZ-Range (RI EZ-Grip, RI EZ-Strip, RI EZ-Squeeze, RI EZ-Tip)
- IVF Pasteur Pipets
- The Stripper Tips (Individual or Multi Pack)
- Incubators
- K-Systems G210 InviCell*
- K-Systems G185*
- ORIGIO ® / PLANER Benchtop Incubator BT37
- Workstations – Class I
- K-Systems 100 Series (L124 / L124 ICSI/ L126 MP)*
- ORIGIO Fortuna
- ORIGIO Titan
- Workstations – Class II
- K-Systems L234 CellTouch*
- K-Systems G603 Work Chamber*
- ORIGIO Mars
- Security & Management
- RI Witness ™

Cryopreservation

- Carrier
- VitriFit ™ *
- CryoLeaf
- VitriGuard (US only)
- **Vitrification & Warming Kits**
- SAGE Vitrification Kit with DMSO
- SAGE Vitrification Warming Kit
- MediCult Vitrification Cooling Kit DMSO free
- MediCult Vitrification Warming Kit
- Slow Freeze & Warming Kits
- CSC Freezing Medium (Oocytes)
- CSC Thawing Medium (Oocytes)
- ORIGIO Oocyte Thaw
- ORIGIO Embryo Freezing Kit
- ORIGIO Embryo Thawing Kit
- ORIGIO BlastFreeze
- ORIGIO BlastThaw
- SAGE Embryo Freeze Kit
- SAGE Blastocyst Freeze Kit
- SAGE Thaw Kit
- Handling Devices
- The Stripper ® (Standard / BP / CC / PGD)
- RI EZ-Range (RI EZ-Grip ®, RI EZ-Strip ®, RI EZ-Squeeze ™, RI EZ-Tip ®)
- IVF Pasteur Pipets
- The Stripper Tips (Individual or Multi Pack)
- Workstations – Class I
- K-Systems 100 Series (L124 / L124 ICSI/ L126 MP)*
- ORIGIO Fortuna
- ORIGIO Titan
- Workstations – Class II
- K-Systems L234 CellTouch*
- K-Systems G603 Work Chamber*
- ORIGIO Mars
- Micromanipulator
- Integra 3 ™ Micromanipulator
- Laser
- Saturn 5 ™ Laser System
- Security & Management
- RI Witness ™

Embryo Biopsy

- Handling Devices
- The Stripper ® (Standard / BP / CC / PGD)
- RI EZ-Range (RI EZ-Grip ®, RI EZ-Strip ®, RI EZ-Squeeze ™, RI EZ-Tip ®)
- IVF Pasteur Pipets
- The Stripper Tips (Individual or Multi Pack)
- Micropipettes
- ORIGIO Biopsy and Holding Pipettes
- TPC Biopsy and Holding Pipettes
- Media
- ORIGIO SynVitro Hyadase
- Biopsy Medium
- Quinn's Advantage ™ medium with HEPES (without Ca/Mg)
- Acidified Tyrodes Solution
- Oil
- ORIGIO Liquid Paraffin
- SAGE Oil
- Micromanipulator
- Integra 3 ™ Micromanipulator
- Laser
- Saturn 5 ™ Laser System
- Workstations – Class I
- K-Systems 100 Series (L124 / L124 ICSI/ L126 MP)*
- ORIGIO Fortuna
- ORIGIO Titan
- Workstations – Class II
- K-Systems L234 CellTouch*
- K-Systems G603 Work Chamber*
- ORIGIO Mars
- Genetic Testing
- PGD
- PGS
- MitoGrade ™
- Genetic Counseling
- Security & Management
- RI Witness ™

Transfer

- Genetic Testing
- PGD / PGS Testing Results
- NIPT
- Transfer Catheters
- Wallace ® Classic Catheter Range
- Wallace ® Sure View ® Range
- Wallace ® Sure-Pro ® Range
- Wallace ® Sure-Pro Ultra ® Range
- ORIGIO Transem Classic Cathether Range *
- ORIGIO EchoGen ™ Ultrasound Range *
- ORIGIO Spherical Tip Catheter *
- ORIGIO Angled Catheter *
- ORIGIO Soft Catheter *
- ORIGIO Supported Catheter *
- Security & Management
- RI Witness ™

Availability of a device for clinical use is dependent on the regulatory approval status within the country the device is intended to be sold into .

Next Generation ART Solutions

CooperSurgical
Fertility and Genomic Solutions

ORIGIO • SAGE • Humagen • TPC • K-Systems
RI • Wallace • LifeGlobal • CooperGenomics

For queries and feedback

Dr (Prof) Pankaj Talwar
Editor Nexus
Secretary General - Indian Fertility Society
E: pankaj_1310@yahoo.co.in, M: +91 9810790063