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IVF & ICSI FAQ

Introduction

The birth of Louise Brown through in vitro fertilization (IVF) on July 25, 1978 in UK by the pioneering efforts of Patrick Steptoe and Robert Edwards dramatically increased public awareness of clinical alternatives for infertile couples. Today, new techniques for assisted reproduction are evolving rapidly by leaps and bounds like never before in history of mankind.

For many couples who have exhausted traditional clinical and surgical treatments for infertility, these techniques may offer the best hope for having pregnancy. Through these procedures many couples with otherwise untreatable infertility have given birth to healthy babies.

In Vitro Fertilization (IVF):

"In Vitro" literally means outside the body. In-Vitro Fertilization (IVF) is a method of assisted reproduction in which fertilization takes place outside the body of a female. Normally fertilization occurs within the fallopian tube and the developing embryo is then transferred through the tube to the uterine cavity in three days by ciliary movements of the cells lining the tube. In IVF, an environment is provided such that the union of the egg and sperm takes place in a petri-dish or test tube under artificial culture conditions in the IVF laboratory. If fertilization occurs, the resulting embryo is transferred to the woman's uterus, where it will hopefully implant in the uterine lining and mature. IVF is a reasonable treatment of choice for couples with various types of infertility.

Indications for IVF:

Female indications:

1. Tubal factor infertility- tubal blockage, hydrosalpinx, absent tubes, tubal adhesions
2. Ovarian factor- resistant cases of polycystic ovaries(PCOD), tubal and ovarian adhesions, premature ovarian failure,
3. Endometriosis
4. Cervical factor infertility
5. Unexplained infertility
6. Immunological infertility

Male indications: These are indications for IVF-ICSI

1. Low sperm count (oligo-zoospermia)
2. Decreased sperm motility (astheno-zoospermia)
3. Abnormal sperm morphology (terato-zoospermia)
4. Techniques requiring surgical retrieval of sperms (TESA, PESA, TESE, MESA)

Basic steps of IVF treatment:

1. Down regulation
2. Controlled ovarian hyperstimulation
3. Egg retrieval or ovum pick up
4. Insemination, fertilization and egg culture
5. Embryo transfer

1. Down regulation:

Ovulation spontaneously occurs during some treatment cycles, despite the use of drugs. When spontaneous ovulation occurs, the eggs may be lost in the pelvic cavity and the cycle must be cancelled. A small percentage of IVF treatment cycles are cancelled because they had either responded poorly to

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ovulation inducing drugs or had premature ovulation. In an attempt to decrease cancellation rates, most of the programmes administer a GnRH analog or antagonist in addition to the other drugs. GnRH analogs are synthetic and modified forms of natural GnRH. Treatment with GnRH analogs prevent the release of LH and FSH from the pituitary gland, and thereby prevents premature ovulation. Cancellation rates as low as 10 percent have been achieved in some IVF programmes using GnRH analogs in combination with other drugs during ovulation induction.

2. Controlled ovarian hyperstimulation (COH) or Super-ovulation:

During ovulation induction, ovulation induction drugs, also known as fertility drugs are used to stimulate the ovaries to produce several mature eggs rather than the single eggs that normally develop each month. IVF specialists agree that the chances for pregnancy are better if more than one egg is fertilized and transferred to the uterus in a treatment cycle. Drug type and dosage vary depending on the patient profile and the stimulation protocol used. Most often the ovulation inducing drugs are given for a period of 10 to 12 days. Ovulation drugs currently in use include clomiphene citrate, human menopausal gonadotrophins (HMG), pure FSH, or recombinant FSH. These drugs may be used alone in combination with others. Clomiphene citrate is given orally while others are given by injections. Usually these injections are started from second or third day of menstrual cycle. Ultrasound is done frequently during treatment cycle to monitor the response of ovaries to the drugs. Drug dose is modified according to the response of ovaries, number and size of developing ovarian follicles which contain eggs. Blood samples are taken to measure the serum levels of estrogen. Normally, estrogen production increases as the follicles develop. Through the use of ultrasound and blood tests, the infertility specialist can determine when the follicles are almost mature. The patient is then given an injection of human chorionic gonadotropin (HCG) for final maturation of the follicles. The HCG replaces the woman's natural LH surge that would normally trigger ovulation in approximately 36 hours. This allows the IVF team to determine the appropriate time for retrieval.

3. Egg retrieval or ovum pick up

Egg retrieval is accomplished by one of the two methods. The first, transvaginal ultrasound guided aspiration, is a minor surgical procedure that is performed under light anesthesia in ovum pick up operation theater which is attached to the IVF laboratory. During this procedure the surgeon guides a small needle through vagina into the ovarian follicles. The eggs (oocytes) are aspirated from the ovarian follicles through the needle with the help of aspiration pump which is set at particular pressure. These collected eggs are then transferred to IVF lab for fertilization. Another method of egg retrieval is through laparoscopy, but this invasive method is not used now days.

4. Insemination, fertilization, egg culture

Once the eggs are retrieved, they are examined in the IVF lab and each one is graded for maturity. The maturity of oocytes determines when the sperm will be added to it (insemination). Insemination can be performed immediately after the oocytes are collected, after several hours or on the following day. On the same day, sperm preparation is done i.e., semen is collected by masturbation, washed and processed, to get rid of the particulate matter and dead sperms by performing the sperm washing procedure. This process helps in obtaining morphologically normal and viable sperms for in-vitro insemination. In the process of insemination, sperms and eggs are put together in a petri-dish or in a test tube containing IVF culture medium and placed in an incubator under controlled environment to allow fertilization. Optimum culture conditions for sperm-egg interaction are provided in the laboratory/culture room for fertilization and embryonic growth.

Fertilization usually takes place in 16 to 18 hours after insemination. About 12 hours after fertilization, the fertilized oocyte (embryo) divides into two cells. The embryo may divide several times while in the

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incubator. The result of successful fertilization is the growth of an embryo to 2, 4, 8, 16-cell stage embryo, morula and blastocyst, which are transferred into the uterine cavity for implantation to successful pregnancy. After 44 to 72 hours, the two to eight cell embryos are ready to be transferred into the woman's uterus. Usually one to three embryos are transferred depending on the grade of embryo, cell stage and uterine conditions. Remaining embryos are cryofreezed for future use.

Another new technique, assisted hatching, is sometimes helpful for women who have undergone IVF previously and have not conceived or for older women undergoing IVF. Assisted hatching is a technique performed after fertilization in which the zona pellucida is thinned or interrupted either chemically or mechanically to facilitate the release of the embryo from the zona. This technique may, in some cases, improve implantation in the uterus.

5. Embryo transfer

The next step in the IVF process is performed on an outpatient basis. No anesthesia is necessary, although some women may wish to have a mild sedative. Using a speculum the IVF specialist exposes the cervix and passes a catheter loaded with the embryo in to the uterine cavity. The embryo is now transferred in to the uterine cavity.

ICSI

Male infertility is mainly due to no sperms, low sperm counts, diminished motility and high percentage of abnormal sperm count. Intracytoplasmic Sperm Injection (ICSI) is the answer to tackle male infertility and failed fertilization in IVF.

In ICSI, a direct injection of a single spermatozoon in a mature oocyte is carried out with help of micromanipulator under inverted microscopic guidance. Semen of male patients is washed and a single sperm, which is morphologically normal, is selected and injected in the oocyte with a very fine needle.

Surgical retrieval of sperms for ICSI: (In patients with azoospermia due to vassal or epididymal blocks)

When semen analysis shows absent sperms but testicular biopsy shows production of sperms in testes then various surgical sperm retrieval techniques are used to retrieve the sperms from testes or the collection system. ICSI treatment is done with these surgically retrieved sperms to achieve the pregnancy. These techniques are

- Testicular sperm aspiration (TESA)
- Testicular sperm extraction (TESE)
- Percutaneous epididymal sperm aspiration (PESA)
- Microepididymal sperm aspiration (MESA)
- Vas deferens aspiration (VDA)
- Spermatocele aspiration

Success rate of IVF-ICSI: The success of conception and pregnancy depends on causes of infertility in a couple, age of female partner, number and grade of embryos transferred, experience of treating doctors, IVF lab standard and many other factors. In our center, the rate of fertilization with ART is 100% with 40 to 45% pregnancy having attained with ICSI, practically over-riding male factor. 30 to 35% is the current rate of pregnancy in our center with conventional IVF procedures. This success rate is comparable with worldwide success rate of IVF. There is of course no specific age limit for couples who may be considered for IVF in our institute.