



ASSISTED REPRODUCTIVE TECHNOLOGY (ART): COMBATING INFERTILITY

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ABSTRACT

Infertility is proving to be a major roadblock in the lives of many couples around the world. If this infertility is overcome it will change the lives of these infertile couples and will help them to have the satisfaction of their own baby without resorting to other means such as adoption. Assisted Reproductive Technology (ART) has evolved immensely in India. Besides the routine infertility treatment by medication, newer avenues have opened for certain invasive techniques which are providing a much higher pregnancy rate and this is helping the couples have their baby sooner and in an easier way. Several useful and highly successful techniques are widely used today such as in vitro fertilization and artificial insemination. The lower price of treatment in India as compared to other countries is resulting in a lot of infertile patients flying down from around the world in their quest of having a baby. Hence, India has emerged as one of the leaders in ART.

Key words: Assisted Reproductive Technology (ART), Artificial Insemination (AI), In-Vitro Fertilization (IVF)

INTRODUCTION

Assisted reproductive technology (ART) is a general term referring to methods used to achieve pregnancy by artificial or partially artificial means. It is a reproductive technology used in infertility treatment, which is the only application of reproductive technology routinely used today. While there is no consensus on the definition, generally the process of intercourse is bypassed either by insemination (example IUI) or fertilization of the oocytes in the laboratory environment (like in IVF).

Medical Procedures¹

Most fertility medications are agents that stimulate the development of follicles in the ovary. Examples are gonadotropins and Gonadotropin Releasing Hormone.

Manual Procedures²

Manual Procedures accounts all forms of ART techniques that use more substantial and forceful interventions than giving medication. In vitro fertilization (IVF) and expansions of it (e.g. OCR, AZH, ICSI and ZIFT) are most prevalent. However there are also other manual ART, but not necessarily dependant on IVF (e.g. PGD, GIFT, SSR). Today, IVF is used to circumvent infertility caused by practically any problem, including endometriosis; immunological problems; unexplained infertility; and male factor infertility. It is a final common pathway, since it allows the doctor to bypass nature's hurdles, and overcome its inefficiency. Due to infertility, married couples opt for ART thus it is important to know the details about infertility such as the different types of infertility, causes and risk factors associated in both men and women.

INFERTILITY

Infertility primarily refers to the biological inability of a man or a woman to contribute to conception. Infertility may also refer to the state of a woman who is unable to carry a pregnancy to full term. Reproductive endocrinologists; the doctors specializing in infertility consider a couple to be infertile if:

- The couple has not conceived after 12 months of contraceptive-free intercourse if the female is under the age of 34.
- The couple has not conceived after 6 months of contraceptive-free intercourse if the female is over the age of 35 (declining egg quality of females over the age of 35, account for the age-based infertility).
- The female is incapable of carrying a pregnancy to term.

SUBFERTILITY

A couple that has tried unsuccessfully to have a child for a year or more is said to be subfertile meaning less fertile than a typical

couple. The couple's fecund ability rate is approximately 3-5%.

Primary vs. Secondary infertility

Couples with primary infertility have never been able to conceive, while, on the other hand, secondary infertility is difficulty in conceiving after already having conceived and to carry a normal pregnancy. Technically, secondary infertility is not present if there has been a change of partners.

CAUSES OF INFERTILITY

Male infertility³

I) Impaired production or function of sperm-

- Impaired shape and movement of sperm.
- Low sperm concentration.
- Varicocele (varicose vein in the scrotum).
- Undescended testicle (cryptorchidism).
- Testosterone deficiency.
- Genetic defects: In the genetic defect Klinefelter's syndrome, a man has two X chromosomes and one Y chromosome instead of one X and one Y. This causes abnormal development of testicles, resulting in low or absent sperm production and possibly low testosterone.
- Infections such as Chlamydia, gonorrhea, prostatitis.

II) Impaired delivery of sperm-

- Sexual issues such as erectile dysfunction, painful intercourse (dyspareunia) or psychological or relationship related issues.
- Retrograde ejaculation:-This occurs when the semen enters the bladder during orgasm rather than emerging out through the penis.
- Blockage of epididymis or ejaculatory ducts.
- No semen (ejaculate).
- Misplaced urinary opening (hypospadias).
- Cystic fibrosis:-Men with cystic fibrosis often have a missing or obstructed vas deferens.

III) General Health and lifestyle

- Emotional stress
- Malnutrition

- Obesity, alcohol and drugs
- Cancer and its treatment
- Age: A gradual decline in fertility is common in men older than 35.

Female infertility ^{2,4}

- **Fallopian tube damage or blockage**
- **Endometriosis**:-Endometriosis occurs during the uterine tissue implants and it grows outside the uterus — often affecting the function of the ovaries, uterus and fallopian tubes. These implants respond to the hormonal cycle and growth, shed and bleed in sync with the lining of the uterus each month, which can lead to scarring and inflammation. Pelvic pain and infertility are common in women with endometriosis.
- **Polycystic ovary syndrome (PCOS)**: In PCOS, the body produces too much androgen hormone which affects ovulation. PCOS is associated with insulin resistance and obesity.

TREATMENT FOR WOMEN

Stimulating ovulation with fertility drugs ⁵

Fertility drugs are the main treatment for women who are infertile due to ovulation disorders. These medications regulate or induce ovulation. In general, they work like natural hormones — such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH) — to trigger ovulation. Commonly used fertility drugs include:

- **Clomiphene citrate (Clomid, Serophene)**:- This drug is most commonly used and is taken orally and stimulates ovulation in women with PCOS or other ovulatory disorders. It causes the pituitary gland to release more FSH and LH, which stimulate the growth of an ovarian follicle containing an egg.
- **Human menopausal gonadotropin, or hMG (Repronex)**
- **Follicle - stimulating hormone or FSH (Gonal - F, Follistim, Bravelle)**
- **Human chorionic gonadotropin or HCG (Ovidrel, Pregnyl)**
- **Gonadotropin - releasing hormone (Gn-RH) analogs**
- **Metformin (Glucophage)**
- **Bromocriptine**

SURGERY

Depending on the cause, surgery may be a treatment option for infertility. Blockages or other problems in the fallopian tubes can often be surgically repaired. Laparoscopic techniques allow delicate operations on the fallopian tubes.

Infertility due to endometriosis often is difficult to treat. Although hormones such as those found in birth control pills are effective for treating endometriosis and relieving pain, they haven't been useful in treating infertility. If endometriosis is detected, the doctor may treat with ovulation therapy, in which medication is used to stimulate or regulate ovulation, or in vitro fertilization, in which the egg and sperm are fertilized in the laboratory and transferred to the uterus.

ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

ART has revolutionized the treatment of infertility. Each year thousands of babies are born as a result of ART. Medical advances have enabled many couples to have their own biological child. An ART health team includes physicians, psychologists, embryologists, laboratory technicians, nurses and allied health professionals who work together to help infertile couples achieve pregnancy.

1. ARTIFICIAL INSEMINATION (AI)

AI is the process by which sperm is placed into the reproductive tract of a female for the purpose of impregnating the female by using means other than sexual intercourse. Specifically, in AI, freshly ejaculated sperm, or sperm which has been frozen and thawed, is placed in the cervix (intracervical insemination) (ICI) or in the female's uterus (intrauterine insemination) (IUI) by artificial means.

Modern techniques for human artificial insemination was first developed for the dairy cattle industry to allow many cows to be impregnated with the sperm of a bull with traits for improved milk production.

1.1 Human artificial insemination ²

In humans, artificial insemination is used as assisted reproductive technology primarily to treat infertility but is increasingly used to enable women without a male partner (i.e. single women and lesbians) to become pregnant and to produce children by using sperm provided by a sperm donor. The woman is the genetic and gestational mother of the child, and the sperm donor is the genetic or biological father of the child.

A sperm sample will be provided by the male partner of the woman undergoing artificial insemination. But sperm donation by a sperm donor may be used if, for example, the woman's partner produces too few motile sperm, or if he carries a genetic disorder, or if the woman has no male partner. When using intrauterine insemination (IUI), the sperm must immediately be "washed" in a laboratory and concentrated in Hams F10 media without L-glutamine, warmed to 37° C. The process of "washing" the sperm increases the chances of fertilization and removes any mucus and non-motile sperm in the semen. Pre and post concentration of motile sperm is counted.

If sperm is provided by a sperm donor through a sperm bank, it will be frozen and quarantined for a particular period and the donor will be tested before and after production of the sample to ensure that he does not carry a transmissible disease. A chemical known as a cryoprotectant is added to the sperm to aid the freezing and thawing process. Further chemicals may be added which separate the most active sperm in the sample as well as extending or diluting the sample so that vials for a number of inseminations are produced.

Procedure

When an ovum is released, fertile semen (provided by the woman's male partner, or by a sperm donor who is a fertile male who is unrelated to, and may be unknown by, the woman), is inserted into the woman's vagina or uterus. In the case of vaginal artificial insemination, semen is inserted into the vagina by means of a needle-less syringe. A longer tube, known as a 'tom cat' may be attached to the end of the syringe to facilitate deposition of the semen deeper into the vagina. The woman is generally advised to lie still for half hour after the insemination to allow fertilization to take place. Alternatively, semen may be placed in the vagina by means of a specially designed cervical cap which holds the semen in place for a period of time, usually for several hours. Using this method, a woman may go about her usual activities while the cervical cap holds the semen in place in the vagina. When semen is inserted into the woman's uterus, only 'washed' semen may be used and this is inserted by means of a catheter. Specially designed equipment is also available for carrying out artificial inseminations. Semen is occasionally inserted twice within a 'treatment cycle'. If the procedure is successful, the woman will conceive and carry to term a baby. A pregnancy resulting from artificial insemination is no different from any other pregnancy but there is a slight increased likelihood of multiples rather than a singleton baby if drugs are used in a 'stimulated' cycle.

Techniques

The easiest way to inseminate is by intracervical insemination (ICI), where semen is injected high into the cervix with a needle-less syringe. This process most closely replicates the way in which semen is deposited by the penis in the cervix when the male ejaculates during vaginal intercourse. However, more technical procedures may be used which increase the chances of conception.

For example, 'washed sperm', that is, spermatozoa which have been removed from most other components of the seminal fluids can be injected directly into a woman's uterus in a process called intrauterine insemination (IUI). If the semen is not washed it may elicit uterine cramping, expelling the semen and causing pain, due to content of prostaglandins.

IUI can furthermore be combined with intratubal insemination (ITI), into the Fallopian tube although this procedure is no longer generally regarded as having any beneficial effect compared with IUI. ITI however, should not be confused with gamete intrafallopian transfer, where both eggs and sperm are mixed outside the woman's body and then immediately inserted into the Fallopian tube where fertilization takes place. IUI is the most popular form of artificial insemination.

2. IN- VITRO FERTILIZATION (IVF)

IVF is a major branch of ART. It is a process by which egg cells are fertilized by sperm outside the woman's womb i.e. in vitro. IVF is a major treatment in infertility when other methods of assisted reproductive technology have failed. The process involves hormonally controlling the ovulatory process, removing ova (eggs) from the woman's ovaries and letting sperm fertilize them in a fluid medium. The fertilized egg (zygote) is then transferred to the patient's uterus with the intent to establish a successful pregnancy.

A colloquial term for babies conceived as the result of IVF, test tube babies, refers to the tube-shaped containers of glass or plastic resin, called test tubes. However IVF is usually performed in the shallower containers called petri dishes. (Petri-dishes may also be made of plastic resins).

History ²

The first pregnancy achieved following in vitro human fertilization of a human oocyte was reported in The Lancet from the Monash Team in 1973, although it only lasted a few days and would today be called a biochemical pregnancy. The first Indian doctor to produce a test tube baby was Dr. Indira Hinduja. On August 6th, 1986, India's first test tube baby, Harsha was born thanks to the three years of painstaking research in in vitro fertilization and embryo transfer.

Procedure ^{2,6}

Ovarian stimulation or superovulation

Treatment cycles are typically started on the third day of menstruation and consist of a regimen of fertility medications to stimulate the development of multiple follicles of the ovaries. In most patients injectable gonadotropins (usually FSH analogues) are used under close monitoring to frequently check the estradiol level. The gynecologic ultrasonography checks the follicular growth. Typically approximately 10 days of injections will be necessary. Spontaneous ovulation during the cycle is prevented by the use of GnRH agonists or GnRH antagonists, which block natural surge of luteinizing hormone (LH).

Egg retrieval

When follicular maturation is judged to be adequate, human chorionic gonadotropin (β -hCG) is given. This agent, which acts as an analogue of luteinising hormone, would cause ovulation about 36 hours after injection, but a retrieval procedure takes place just prior to that, in order to recover the egg cells from the ovary. The eggs are retrieved from the patient using a transvaginal technique involving an ultrasound-guided needle piercing the vaginal wall to reach the ovaries. The ultrasound probe is inserted through the vagina. The probe emits high-frequency sound waves which are translated into images of the pelvic organs and displayed on a monitor, so that the mature follicles can be seen as black bubbles on the screen. The doctor guides a needle through the vagina into each mature follicle. The follicular fluid containing the egg is then sucked out through the needle into a test tube, and all the follicles are aspirated, one by one. This is a very precise procedure, which requires considerable skill, and takes about 10-40 minutes to perform, depending upon the number of eggs. On an average, about 4-16 eggs are retrieved for each patient. If there are few eggs, each follicle is flushed, to ensure

that each egg is retrieved. The follicular fluid is handed to the IVF laboratory to identify ova.

Selection ^{2,3,7}

Laboratories have developed grading methods to judge oocyte and embryo quality. Typically, embryos that have reached the 6-8 cell stage are transferred three days after retrieval. In several latest developments embryos are placed into an extended culture system with a transfer done at the blastocyst stage, especially if many good quality 3 day embryos are available. Blastocyst stage transfers have shown to result in higher pregnancy rates.

Embryo Transfer ³

Embryo transfer is most often done on an outpatient basis. No anesthesia is used, although some women may wish to have a mild sedative. The patient lies on a table or bed, usually with her feet in stirrups. Using a vaginal speculum, the doctor exposes the cervix. One or more embryos suspended in a drop of culture medium are drawn into a transfer catheter, a long, thin sterile tube with a syringe on one end. Gently, the doctor guides the tip of the loaded catheter through the cervix and deposits the fluid containing the embryos into the uterine cavity. The procedure should be done with great care and usually takes between 10 and 20 minutes. Some doctors perform the transfer under ultrasound guidance, to ensure proper placement of the embryos in the uterine cavity. Most doctors advise a few hours of bed rest after the transfer.

Most clinics today transfer 2-3 good quality embryos on Day 2 or Day 3. Embryos are graded according to their appearance and rate of cell-division and good quality embryos are those which have 4-8 cells, of equal size, with clear cytoplasm, and with few fragments. These are called Grade A embryos. Embryos with more fragments are assigned a lower grade, and they usually have a lower chance of implanting. However, the babies who result from these embryos are completely normal, if they do implant successfully.

EXPANSIONS OF IVF ²

ICSI

Intracytoplasmic Sperm Injection (ICSI) is a more recent development associated with IVF which allows the sperm to be directly injected in to the egg. With ICSI the equation "1 egg plus 1 sperm = 1 embryo". This is used in cases of male infertility where sperm have difficulty penetrating the egg and in this case the partner's or a donor's sperm is used. ICSI is also used when sperm numbers are low. ICSI results in success rates are equal to IVF fertilization.

GIFT

Gamete intrafallopian transfer (GIFT) is a popular alternative to IVF in the past. A gamete is a male or female sex cell - a sperm, or an egg. During GIFT, sperm and eggs are mixed and injected into one or both fallopian tubes. After the gametes have been transferred, fertilization can take place in the fallopian tube as it does in natural, unassisted reproduction. Once fertilized, the embryo travels to the uterus by natural processes.

ZIFT

Zygote intrafallopian transfer (ZIFT) is also called PROST, which stands for pronuclear stage transfer. When a sperm penetrates an egg, the sperm introduces its nuclear material into the egg. Approximately 14 hours after penetration, two distinct pronuclei, one from the sperm and one from the egg, are visible under the microscope. Pronuclei are taken as indicators that fertilization has occurred. A zygote is a fertilized egg before cell division begins. For ZIFT, eggs are removed by transvaginal aspiration and fertilized in a laboratory dish. The next day, when the fertilized eggs have reached the pronuclear stage, the embryos are transferred to the fallopian tubes during laparoscopy.

Approximately 24 hours after a fertilized egg reaches the pronuclear stage, it divides for the first time and becomes a two cell embryo. This cell division is called cleavage. It is at this stage or later that tubal embryo transfer (TET), may be attempted. The fertilized and

dividing egg (early cleavage stage embryo) is transferred to the fallopian tube during laparoscopy.

AZH

One of the major problems with IVF today is the low pregnancy rate after successful embryo transfer. Dr. Cohen from New York believes this is because the surrounding shell of the embryo (called the zona pellucida) hardens when it is cultured in the laboratory. They therefore use "embryo surgery" called zona drilling or assisted zona hatching (AZH) to "soften" the shell of the embryo, and they believe this helps to increase pregnancy rates by improving implantation rates, since embryo hatching is facilitated. This can be done using an acid or a laser.

PGD

Preimplantation genetic diagnosis (PGD) is a new technique, which marries the recent spectacular advances in molecular genetics and assisted reproductive technology. Preimplantation genetic diagnosis enables physicians to identify genetic diseases in the embryo, prior to implantation, before the pregnancy is established. Sexing the embryo to avoid X linked disease remains the commonest reason for preimplantation diagnosis, now optimally carried out by the molecular cyto genetic technique of FISH (fluorescent in situ hybridization) with DNA probes derived from the X and Y chromosomes.

RISKS AND COMPLICATIONS OF IVF^{2,8}

Ovarian hyperstimulation syndrome (OHSS)

The most complication of IVF is that of OHSS because of superovulation. The cause of "hyperstimulation syndrome" is that superovulated ovaries contain many follicles which are loaded with estrogen. After ovulation, a huge amount of estrogen-rich fluid is poured directly out of the enlarged and fragile ovaries into the abdominal cavity. This fluid also contains chemicals like kallikrein-kinin and VEGF (vascular endothelial growth factor), which then coat the lining of the abdominal cavity (called the peritoneum) and cause it to become very permeable (leaky).

Fluid (serum) literally pours out of your bloodstream into the peritoneal cavity because of the "leakiness" of the abdominal cavity's lining. The ovaries balloon in size, abdomen swells, one gets lightheaded with relatively low blood pressure, and may result in dizziness because of the decreased blood volume.

Multiple Pregnancy⁹

In all techniques of assisted reproductive technology, the chance of multiple pregnancy is increased when more than one embryo or egg is transferred. A recent treatment option for women with multiple pregnancies is that of selective fetal reduction, in which one or more of the fetuses are selectively destroyed (usually by injecting the toxic chemical, potassium chloride, into its heart under ultrasound guidance). In most cases, the killed fetus is then reabsorbed by the body - and the other fetuses continue to grow. Of course, the risk of all the fetuses being lost because of a miscarriage is also present.

Emotional Aspect

Couples undergoing IVF and GIFT have described the experience as an emotional roller coaster. The treatments are lengthy, and costly. These procedures often create high expectations but are more likely to fail than to succeed in a given cycle. The unsuccessful couples will feel frustrated in their quest for pregnancy. At times, this feeling of frustration leads to depression and feelings of low self-esteem.

DONORS^{2,10,11}

Egg donor

Egg donation is the process by which a woman provides one or several eggs (ova, oocytes) for purposes of assisted reproduction or biomedical research. For assisted reproduction purposes, egg donation involves the process of in vitro fertilization as the eggs are fertilized in the laboratory. After the eggs have been obtained, the role of the *egg donor* is complete. Egg donation is part of the process of third party reproduction.

Egg donors are recruited, screened, and give consent prior to participation in the IVF process. Some patients bring their own, *designated donors*, while other patients rely on the services of often *anonymous donors* typically recruited by *egg donor agencies* or, sometimes, IVF programs. Once the egg donor is recruited, she undergoes the IVF stimulation therapy, followed by the egg retrieval procedure. After retrieval, the ova are handed over to the recipient couple, fertilized by the sperm of the male partner in the laboratory, and after several days, the resulting embryo(s) is placed in the uterus of the recipient. For the embryo transfer the lining of the recipient has been appropriately prepared in a synchronous fashion. The recipient is usually the person who requested the service and then will carry and deliver the pregnancy and keep the baby.

Sperm Donor

Sperm donation is the name of the practice by which a man, known as a sperm donor, provides his semen with the intention that it be used to produce a baby where the man does not have sexual relations with the recipient of his semen. Attempts are made to impregnate a woman with the donor's sperm using third party reproduction techniques notably artificial insemination.

A sperm donor may donate his sperm directly to the woman recipient, or he may donate it at a clinic known as a sperm bank. Sperm provided in this way is known as donor sperm.

Sperm donation commonly assists couples unable to produce children because of 'male factor' fertility problems, but it is increasingly used as a means to enable single women (termed choice mothers) and single and coupled lesbians to have their own children. The sperm donor is the genetic or biological father of each child produced with the use of his sperm. When a donor's sperm is successfully used repeatedly for impregnation, number of siblings and half-siblings will be produced. Donors are also paid for the sperm donation depending on the quality of the sperm. Lack of awareness results in lesser sperm donations in India.

Couples seek 'perfect donors' for designer babies¹¹

Rich and upper middle-class infertile couples in their quest for the perfect baby are soliciting eggs from young women through newspaper advertisements which typically read: "Wanted an egg donor for rich couple. The donor will be handsomely compensated."

The practice is in violation of the guidelines of the Indian Council of Medical Research (ICMR) on assisted reproductive technologies under which an infertile couple is not supposed to know the identity of the donor. The guidelines prohibit a couple from seeking a sperm or an egg donor, stating that seeking donors is the responsibility of ART clinics.

Couples are very choosy and want eggs from young women whose social profile and physical attributes closely match theirs. They even look for a proper caste and sub-caste which would match theirs. Some parents are very particular about the color of the eye or hair. They want the child to resemble them as much as possible.

Experts say that these couples forget that ART has a success rate of just 35%¹². Given such a low rate, couples should hope to have a baby, any baby, instead of seeking a designer baby.

Surrogate Mothering⁴

Surrogacy is a method of reproduction whereby a woman agrees to become pregnant and deliver a child for a contracted party. She may

be the child's genetic mother (the more traditional form of surrogacy), or she may, as a gestational carrier, carry the pregnancy to delivery after having been implanted with an embryo. Surrogacy is a controversial, and in some jurisdictions, illegal, medical procedure.

RECENT DEVELOPMENTS of ART in INDIA

A new test can now detect if the eggs produced by a woman are defective which may prove to be a boon for women who opt for IVF. Till now women would routinely subject themselves to a series of failed IVF attempts without realizing they carried defective eggs, which would produce abnormal children.

It is conducted in the following manner: A healthy egg contains a spindle which holds the complete genetic package. Some eggs don't contain it. A special imaging system called the spindle view, in use abroad since 2003 and now available in India, makes it easy to check it. If there's no spindle, either the woman has a miscarriage or the baby is abnormal, with defects like Down's syndrome or cerebral palsy.

- **Vitrification** ^{10, 13}

This technique called vitrification was first successfully conducted in humans in Japan. The procedure involves the embryos being mixed with a freezing media and suddenly plunged into liquid nitrogen. The super high concentration of anti freeze and rapid drop in temperature prevents the water in the cells from turning into ice. The entire embryo goes into glassy state, avoiding the ice crystals, which are known to damage the embryo.

Preservation techniques till now had a low rate of about five to six eggs and the rest had to be destroyed. This was primarily because of the formation of ice crystals which damaged the eggs which were frozen by the slow freezing process. Now because of the vitrification process the eggs can be preserved indefinitely if the 196° C temperature is maintained.

- **IMSI 12**

Intracytoplasmic Morphologically Selected Sperm Injection (IMSI) is a modified form of ICSI; however the only difference is that it carefully selects the best quality sperm by magnifying it 7200 times as compared to 200 times in the conventional ICSI method. Patients with severe low sperm count can benefit from IMSI.

- **Intravaginal culture 10**

Vaginal Incubation

Incubating the eggs and embryos in vitro requires expensive CO₂ incubators, which must maintain just the right environment for the embryos for long periods of time. The method of intravaginal culture (IVC), however, allows one to provide IVF services without using a CO₂ incubator and is an extremely attractive alternative. Basically, in IVC the eggs and sperm are placed in culture medium in a sterile vial which is hermetically sealed and then placed in the woman's vagina where it is held in place with a vaginal diaphragm. This means that the woman acts like her own IVF incubator and keeps her embryos at the right temperature 37° C. This method requires less handling of eggs and embryos and provides a fertilization rate comparable to that of conventional IVF - at much less expense.

Encapsulated Gametes

Another innovation in this field has been the concept of encapsulated gamete intrauterine transfer in which the eggs and sperm are transferred into the uterine cavity after placing them in a biodegradable semipermeable matrix. The capsule acts functionally like a temporary incubator chamber which prevents the egg from being damaged as a result of direct contact with the endometrium. After fertilization has occurred in the cavity, the capsule dissolves and releases the embryos for implantation. If this technique lives up to its promise, then many more centers will be able to provide assisted conception services to their patients.

CONCLUSION

ART is a treatment option for couples with various types of infertility. It allows the doctor to perform in the laboratory what does occur in the natural way. It allows the doctor to bypass nature's hurdles, and overcome its inefficiency, so that we can give Nature a helping hand. There has been a gradual increase in awareness and

the benefits of this technology are fast catching up with couples unable to conceive naturally. The cost still proves to be a major deterrent but there have been steady improvements which involve cost cutting without deterioration in the quality of the treatment ¹⁴.

The dark side of this journey of having a baby does exist. Malpractices on the part of the ART clinics who indulge in illegal activities like sex determination. Donors make the process of egg donation a business and even the couples sometimes not ethically abide by the law in the quest to have a perfect baby. It has now become extremely essential that the laws be strictly enforced to keep a check on these activities.

Till date couples unable to have a baby would go in for adoption as a last resort to have a baby but with ART these couples have a ray of hope and has proved to be a major boon for them.

REFERENCES

1. Goodman & Gilman. The Pharmacological Basis of Therapeutics. 11th Edition. McGraw-Hill Professional; 1984.
2. Dr. Aniruddha Malpani, MD and Dr. Anjali Malpani, MD. How to Have a Baby: Overcoming Infertility. Rajkamal Electric Press, Delhi; 2001.
3. De Jonge CF and Barratt CLR, editors. Assisted Reproductive Technology: accomplishments and new horizons. New York: Cambridge University Press; 2002; pp.431.
4. Parks JA. A closer look at reproductive technology and postmenopausal motherhood. CMAJ 1996; 154(8):1189-1191.
5. Golan and Armstrong. "Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy." Second Edition.
6. Brinsden PR and Rainsbury PA, editors. A textbook of In Vitro Fertilization and Assisted Reproduction. The Bourn Hall Guide to clinical and Laboratory Practice; Second Edition, The Parthenon Publishing Group Inc.; 1999.
7. Papanikolaou EG, Camus M, Kolibianakis EM, Van Landuyt L, Van Steirteghem A, Devroey P. In Vitro Fertilization with Single Blastocyst-Stage versus Single Cleavage-Stage Embryos. N Engl Med J 2006; 354(11):1139-1146.
8. Zhang Y, Zhang YL, Feng C, Wu YT, Liu AX, Sheng JZ, Cai J, Huang HF. Comparative proteomic analysis of human placenta derived from assisted reproductive technology. Proteomics 2008; 8(20):4344-4356.
9. Kurinczuk JJ, Hansen M, Bower C. The risk of birth defects in children born after assisted reproductive technologies. Curr Opin in Obstet and Gynecol 2004; 16(3):201-209.
10. The Times of India, 2008.
11. Daily News and Analysis, 2008
12. Van Voorhis BJ. Clinical practice. In vitro fertilization. N Engl J Med 2007; 356(4):379-386.
13. Porcu E, Fabbri R, Damiano G, Fratto R, Giunchi S, Venturoli S. Oocyte cryopreservation in oncological patients. Eur J Obstet Gynecol Reprod Biol 2004; 113(1):S14-6
14. Hansen M, Bower C, Milne E, Klerk N, Kurinczuk JJ. Assisted reproductive technologies and the risk of birth defects-a systematic review. Hum Reprod 2005; 20(2):328-338.