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In vitro Fertilisation and Other Artificial Reproductive Technology Methods-Review Paper

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Abstract: Technology in human assisted reproduction has certainly shown great advances during the past couple of decades. *In Vitro* Fertilisation (IVF) is only one of those techniques which are offering infertile couples the possibility of experiencing parenthood. Infertility affects one's life at the very core-feelings of anger, depression and guilt are very commonly experienced by infertile couples. The causes of infertility are many; amongst the most common are blockages of the fallopian tubes, endometriosis, low sperm counts and poor sperm motility and/or morphology. IVF, however, is not the answer to all fertility problems. IVF is mostly suitable in those cases where there are fallopian tube problems or cervical mucus which is hostile to sperm, since in IVF both the passage of the ovum through the fallopian tube and the passage of sperm through the cervix are by-passed. There are various alternatives to IVF, such as Artificial Insemination (AI) and Gamete Intrafallopian Transfer (GIFT). The latest innovative technique, Intracytoplasmic Sperm Injection (ICSI), which in the future might replace traditional IVF involves the injection of sperm directly into the ovum and is hence ideal for those cases with severe male factor infertility. The setback with all the advances that are being witnessed in assisted reproduction is that they also give rise to many ethical questions. Different countries, with different social, legal, religious and moral backgrounds have different opinions regarding the research on embryos, third-party parenting and gamete/embryo freezing. This study describes the main procedures, techniques and equipments that are used in IVF and its alternatives, as well as the benefits and the ethical implications that such techniques give rise to.

Key words: *In vitro*, fertitisation, artifical, GIFT, ICSI, IVF

INTRODUCTION

Whether being medical, social, religious or political, *In Vitro* Fertilisation (IVF) has been a very important and discussed issue for many years now. The first test-tube baby, Louise Brown, was born in England in 1978, however experiments and studies involving embryology have much longer histories. The first embryo transfer was carried out in rabbits by the English scientist, Walter Heape, way back in 1890 (Leese, 1988). In his experiment, Heape was studying whether a uterine foster-mother would have any effects upon her foster children (rabbits). The result to this experiment was obviously negative, however, in the meantime, Heape had discovered how to remove a fertilised ovum prior to implantation from one animal and transfer it into the uterus of another animal of the same species, with the consequent production of healthy offspring.

In 1934, Pincus and Enzmann transferred supposedly fertilised ova into a rabbit's uterus following IVF, with the result that the born offspring had the same physical characteristics as those expected by the scientists (Leese, 1988). However, Pincus and Enzmann allowed the eggs only thirty minutes *In vitro* before being transferred and hence scientist claimed that the transferred eggs may have had viable spermatozoa adhered to them, in which case the fertilisation would have taken place *In vivo* (i.e., in the uterus) rather than *In vitro* (i.e., in the Petri dish). These doubts were cleared in 1959, when M.C. Chang allowed the fertilised ovum to divide up to the four-cell stage *In vitro* before transferring the embryo, such that any spermatozoa attached to the transferred embryo would have lost their capacity of fertilising an ovum. Any further discussions and disagreements where later put to a halt in 1978 by the birth of Louise Brown (Leese, 1988).

But what does *In vitro* Fertilisation comprise? The literal meaning of *In vitro* fertilisation is fertilisation in glass, however the actual process involves much more than it is implied by this meaning. First, the correct amounts and combinations of fertility drugs are administered to the woman. These enhance the maturation of several eggs in the woman's ovaries. Then, mature ova are obtained by suction, a process which involves the

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insertion of a needle into the woman's ovary. After obtaining a semen specimen from the donor or husb and this specimen undergoes sperm washing and capacitation, such that the spermatozoa are made viable to fertilise an ovum. Fertilisation is then carried out in a Petri dish, in which the embryo or embryos divide repeatedly for a number of days. This is then followed by embryo transfer i.e., an embryo or several embryos are transferred into the woman's uterus, by means of a thin catheter, such that the embryo or embryos can implant themselves in the endometrial lining (Sher *et al*., 1995).

In vitro Fertilisation can be the solution to various infertility problems, but not to all. This implies that the cause of infertility should be very well identified before administering any type of treatment to a patient. Furthermore, IVF involves various ethical issues which will also be discussed.

Infertility: Infertility is described as the lack of conception after one year of unprotected intercourse (Bayer *et al*., 2002). Considering that there is an approximate 15-20% chance per month of achieving pregnancy and that about 73-80% of couples achieve pregnancy before six months of trying, it is justified that an infertility evaluation and treatment are initiated after six months rather than one year.

Infertility *per se* is not very common, affecting about 5-8% of the population in developed countries (Bittles and Matson, 2000). What is more common, however, is the loss of early pregnancies. Various studies were carried out on women who had experienced an early abortion and certain trends in the results of these studies persisted from month to month. It was in fact observed that in any one month under normal conditions:

- 15% of oocytes fail to undergo fertilisation
- 10-15% of oocytes become fertilised and cleave, but fail to implant
- only 42% of implanted ova succeed in suppressing the following menstrual period
- a further 24% lose their foetus after week four of gestation (Bittles and Matson, 2000).

New reproductive technologies are providing approximately 80% of infertile couples who seek treatment with offsprings which are genetically related to both parents, whereas another 10-15% are also provided with pregnancy however using donated gametes (i.e., offspring would be related to only one or none of the parents) (Fishel *et al*., 2000). Infertility, although a medical problem, also involves many other issues including psychological, legal, moral and social issues and hence administering the proper treatment becomes even more difficult.

Factors affecting fertility: Several factors affect reproductive physiology. Some, like maternal age, cannot be avoided but many others such as smoking and caffeine can be avoided by leading a healthy life-style.

An important factor is maternal age. As the woman gets older, her oocyte quality declines and therefore oocytes become more susceptible to meiotic and mitotic errors. This increased chance of chromosomal errors in older women has therefore increased the rate of spontaneous abortions, as well as the birth of babies with genetic defects such as Down's syndrome. The discontinuation of contraception may also interfere with fertility, an important example being Intra-Uterine Devices (IUDs) which greatly increase the risk of pelvic inflammatory disease. Smoking is another important factor since it directly affects enzymes necessary for the production of ovarian hormones and in men, it reduces sperm motility and concentration.

Causes of infertility: In about 45% of infertile couples, the cause of infertility lies within the female. In 30% of cases, there is male factor infertility whereas the remaining 25% are unexplained (Bayer *et al*., 2002).

When the cause of infertility lies within the female, there are great chances that the problem is ovulatory. This means that the woman might not be ovulating at all and would be evident when her menstrual cycle is irregular (the regular menstrual cycle is 23-39 days in length). Anovulatory cycles occur when the pre-ovulatory surge of LH is not of sufficient magnitude to cause ovulation (Guyton and Hall, 2000). This type of problem is treated by administering hormones, such as, Gonadotropin-Releasing Hormone (GnRH), Human Menopausal Gonadotropin (HMG) and Follicle-Stimulating Hormone (FSH), depending on the problem (Bayer *et al*., 2002). Other problems include cervical mucus which is hostile to sperm, blockages of one or both the fallopian tubes and uterine dysfunction. IVF is ideal in those case where there is blockage of the fallopian tubes, since the procedure by-passes these structures. A hysterosalpingogram, on the other h and, would demonstrate uterine problems such as sub-mucosal fibroids, intra-uterine adhesions or a bicornuate uterus (Leese *et al*., 1988).

When infertility lies within the male, very often it is due to oligospermia i.e., a low sperm count. Although very uncommon, azoospermia i.e., no sperm production is also possible. Abnormal morphology or poor sperm motility would also hinder fertility, even in those cases where the sperm count appears to be normal. Genetic defects, such as Kleinfelter's syndrome and Kallmann's syndrome, may also be the cause of male infertility (Bittles and Matson, 2000).

This wide variety in the causes of infertility underlines the importance of a complete and accurate Infertility Evaluation. Unless the cause is identified, treatment cannot be commenced.

IVF procedures: In most instances where first-line treatments such as ovulation induction, intrauterine insemination and surgical interventions are of no success, IVF remains to many couples the only hope of achieving pregnancy. Prior to IVF treatment, a couple should be well informed about what IVF consists of, as well as about the emotional and financial commitments that are involved.

The first step in IVF is to artificially induce ovulation of more than one egg using fertility drugs. This step is fundamental to IVF since the success rate strongly depends on the number of eggs that are retrieved. Ovulation occurs approximately 38 to 42 h after the administration of fertility drugs and since eggs need to be retrieved before they are released into the abdominal cavity, it is absolutely necessary that the development of the follicles is monitored (Sher *et al*., 1995). Amongst the most commonly used fertility drugs are clomiphene citrate, which is administered orally and HMG, which is given as a subcutaneous injection. Furthermore, the woman would not ovulate until an injection of human Chorionic Gonadotropin (hCG) is later administered. hCG is given intramuscularly when at least one follicle is greater than or equal to 18 mm in diameter (Elder and Dale, 2000) and will promote the final changes in the eggs that are necessary for egg retrieval. In order to determine when to inject the hCG necessary for the final maturation of eggs and when to perform egg retrieval, the development of the follicles in response to the administered fertility drugs must be tightly followed. This is performed by measuring estradiol levels and by means of ultrasound examinations (Bayer *et al*., 2002). Finally, in order to increase the likelihood that implantation will take place, the administration of progesterone is commenced the day after the hCG injection is given. This is required to maintain the secretory endometrium during the luteal phase and pregnancy. Different formulations exist, some of which are given *per vaginum* whereas others are administered as an intramuscular injection, such as Utrogestan capsules and Gestone, respectively (Germond *et al*., 2002).

Egg retrieval is usually performed 34-36 h after the hCG injection (Elder and Dale, 2000). This procedure makes use of disposable sterile needles for aspiration of the follicles, a sterile ultrasound probe which transmits the image of the ovarian follicles to the viewing monitor (Sher *et al*., 1995) and heated 15 mL Falcon tubes for the collection of the aspirated follicles (Elder and Dale, 2000). For safety precautions, egg retrieval must be carried out under intravenous sedation or light general anaesthesia (Elder and Dale, 2000). In addition, a paracervical block may also be performed; this involves the injection of local anaesthetic in the cervical region and will thus avoid the patient any feelings of pain (Sher *et al*., 1995). Egg retrieval is performed transvaginally; first the probe is introduced so that an image is produced on the viewing monitor and then the sterile needle will follow the same route until it reaches the ovarian follicles. Aspiration of the follicles then follows (Sher *et al*., 1995). The whole procedure is considered to be a safe one and patients are usually discharged within a couple of h after termination of the procedure. After each egg reaches maturity, these are placed in a separate Petri dish containing a fluid which is of nourishing value to the eggs. Among the most important constituents of this fluid is sodium bicarbonate, which acts as a buffer, neutralising those waste products produced by the egg which would tend to alter the surrounding pH. For sodium bicarbonate to act as a buffer it needs aconstant supply of carbon dioxide and this explains why the retrieved eggs are incubated in an environment containing 5% carbon dioxide (Sher *et al*., 1995).

When performing IVF, the passage of sperm through the vagina and uterus up to the fallopian tube is bypassed since the fertilisation process occurs in a Petri dish rather than in the fallopian tube. Therefore, if insemination is to be successful, then the semen specimen needs to undergo capacitation in the laboratory. The first step to be performed is sperm washing, which refers to the separation of spermatozoa from seminal fluid. This has to be performed as soon as possible after ejaculation since it was found that prolonged exposure of spermatozoa to seminal fluid decreases both sperm motility and viability (Drobins, 1997). The ideal method for sperm washing should be able to produce a high concentration of spermatozoa with high motility, intact plasma membranes, high zona-binding ability and intact acrosomes. The swim-up technique is a simple procedure which meets these dem ands (Berger *et al*., 1995). The semen sample is first diluted with an equal volume of Biggers-Whitten Whittingham (BWW) and after centrifugation at 300 g for 10 min, the supernatant is discarded whereas the pellet is resuspended in 2 mL of BWW. Centrifugation and resuspension are repeated until 0.3% Bovine Serum Albumin factor V (BSA) is added to a final volume of 600 μL. About 200 μL of this sample are then placed in a tube, beneath a layer of 800 μL BWW supplemented with 0.3% BSA. This is then followed by incubation at 37°C, under 5% carbon dioxide and at a 45° angle for 1 h. This will allow spermatozoa to migrate from the lower layer to

the upper layer. Subsequently, the top 600-700 μL is removed with extreme care to avoid disrupting the interface of the two layers. The supernatant must thus contain actively motile spermatozoa (Esteves *et al*., 1999). Capacitation is then performed by incubating the sample in a BWW medium with 3% BSA at 37°C, under 5% carbon dioxide in air for 3 h (Henkle *et al*., 1993). Only after the performance of these treatments are the sperm ready to fertilise an ovum. Such techniques are very advantageous since they select a sperm population with those characteristics ideal for fertilisation.

For fertilisation to take place, the oocyte and spermatozoa must be brought into close proximity. The higher the concentration of healthy spermatozoa, the greater the chances that insemination is successful; in fact, the insemination concentration usually contains 100,000 normal motile sperm per millilitre (Elder and Dale, 2000). After incubating the oocytes for 3-4 h under the previously mentioned conditions, each oocyte is transferred into a drop of spermatozoa. Fertilisation usually takes place within the first few h, but still the mixture is left in the incubator overnight, at 5% carbon dioxide and 37°C temperature. After 16-20 h (Sher *et al*., 1995) the eggs are examined for fertilisation; this involves dissection of the embryo since, by now, the corona radiata would have condensed to prevent fertilisation by more than one sperm but also, at the same time, preventing the embryologist from observing the fertilised egg's contents. This procedure makes use of a small-gauge syringe needle or a fine-bore glass pipette (Sher *et al*., 1995) and is a very delicate one since extreme care must be taken not to expose the fertilised eggs to any changes in temperature or pH. At this point, fertilisation is confirmed if two pronuclei can be observed. If any abnormality is detected, then the embryo wouldn't be suitable for implantation. Among the most common abnormalities are polysermia i.e., when more than one sperm penetrate the ovum and nonextrusion of the second polar body. Furthermore, any surplus embryos possessing two pronuclei can be cryopreserved, especially if the patient has a history of poor embryo cleavage and implantation rates (Elder and Dale, 2000).

Finally embryo transfer is performed, usually on day 2 or day 3 after insemination (Mortimer, 1995). A speculum is used to view the opening of the cervix, whereas a special medium is used to clean the vaginal canal and cervix. The bladder needs to be full since it allows good visualisation of the catheter thereby making the transfer of the embryos smoother and to the best location and also because it unfolds the uterus to a more accommodating angle and hence the process is less traumatic for the endometrial lining. The embryologist's role is to load the catheter with the embryo or embryos whereas the physician will pass the catheter through the cervical opening up to the middle of the uterine cavity. Once the correct location is reached, the embryos are squirted out of the catheter, usually by the embryologist (Edwards, 1992). After withdrawing the catheter, it is checked under a microscope for any retained embryos. The patient needs to lie down for about 1 h after the procedure and it is usually recommended that she limits physical activity for the rest of the day.

Expectations from and alternatives to IVF: When selecting the fertility practice where to seek treatment, one factor that any couple would surely want to consider is the success rate. Unfortunately, in the case of IVF, success rates are quite a confusing subject. This is because success rates vary considerably from couple to couple, depending on diagnosis, prior IVF treatments, duration of infertility and, most importantly, age. All these affect the potential for a successful pregnancy following fertility treatment. As a woman's age increases, her chances at becoming pregnant through assisted reproduction decrease, mainly due to diminishing egg quality (Romeau *et al*., 1987). The live birth rate among women beginning assisted reproduction cycles after age 40 is often as low as 10-20% (Lim and Tskok, 1997). In some cases, the only option for women trying to conceive a child later on in life is the use of a donor egg. Furthermore, success rate values depend on how success is defined and how the total population is calculated. One must make a clear distinction between clinical pregnancy rate (i.e., implantation seen by ultrasound), ongoing pregnancy rate (i.e., foetal heart beat seen by ultrasound) and the actual delivery of a baby. Most couples seeking infertility treatment wouldn't be acquainted with medical terms and hence an explanation of such terms should be given prior to the initiation of the treatment. Unfortunately, infertile couples will encounter different success rates from one clinic to another and the best success rate may not necessarily provide a particular couple with the best chances for achieving pregnancy, since each couple is unique and has a unique set of circumstances. A realistic statistic would be one that takes into account a mix of patients i.e., both ideal ones, who are young, have had previous pregnancies, have regular menstrual cycles and normal sperm factors, as well as difficult patients, who have perhaps failed in previous IVF treatments, are over 38 years of age, have borderline FSH values, prolonged unexplained infertility and are low responders to medications (Larsen and Vauper, 1993).

The first step in an IVF cycle involves the development of more than one follicle by injecting

exogenous hormones. Risks associated with injectable fertility medications may include, but are not limited to, tenderness, infection, haematoma and swelling or bruising at the injection site. Further risks may also include allergic reactions, hyperstimulation of the ovaries (which can in turn be mild, moderate or severe), failure of the ovaries to respond and cancellation of the treatment cycle (Zorn, 1995). Cancellation of the treatment cycle is necessary when the ovaries produce either too many or too little oocytes in response to the fertility drugs. This is usually experienced as a huge disappointment by the couple, but it is absolutely necessary in order to avoid complications and to preserve the chance of success with future therapies. As a consequence of the administration of fertility drugs, oestrogen and progesterone levels reach higher than normal levels. The side effects that might be experienced because of this include fluid retention, nausea, diarrhoea, pelvic discomfort (due to enlarged ovaries), breast tenderness, mood swings, headaches and fatigue (Zorn, 1995). Another important risk associated with the administration of fertility drugs is the risk of multiple pregnancies. One cannot neglect the fact that 20-25% of IVF pregnancies are multiple (Zorn, 1995). Multiple pregnancies carry with them an increased risk of miscarriage, premature labour and premature birth, as well as an increased emotional and financial cost. Furthermore, pregnancy-induced high blood pressure and diabetes are more common in women pregnant with more than one foetus.

IVF is not the answer to all fertility problems; although sometimes it is the best option, sometimes it can be the worst. When treating fertility problems, one should always attempt first the least invasive procedures, if these are a possible option. IVF is very often the last option.

Artificial insemination: Artificial insemination is a term that covers a range of techniques, all of which involve the placing of sperm into the female genital tract. Such inseminations may include Intravaginal Insemination (IVI), Intracervical Insemination (ICI), intrauterine insemination (IUI), Intrafallopian Insemination (IFI) and Intraperitoneal Insemination (IPI). The latter two are very rarely performed since they are quite invasive procedures. In IFI, sperm is placed in the fallopian tube whereas in IPI, sperm are placed in the peritoneal cavity next to the opening of the fallopian tube.

IUI is a simpler and cheaper method than IVF; furthermore, IUI has higher success rates than IVI and ICI because in IUI, motile sperm is placed much closer to the fallopian tubes (the site of fertilisation). The success rate of IUI can be further increased if it is combined with ovarian stimulation (Bayer *et al*., 1995). As in IVF, a semen specimen must be obtained, washed and capacitated (Ombelet *et al*., 1995), as well as monitoring of the developing follicle(s). Monitoring is essential since IUI depends very much on the timing of insemination. IUI is done either when ovulation is imminent or just after. There are several methods available for timing insemination in natural cycles. These include: Measurements of basal body temperature (least accurate method), assessment of cervical mucus (not reliable), detection of the LH surge in the urine or blood and ultrasound scans. The latter two are the most commonly used methods since they are the most accurate ones (Ombelet *et al*., 1995). Insemination is usually performed at 24 and 48 h after urine LH surge. For stimulated cycles insemination is usually performed about 40 h after the hCG injection (Berger *et al*., 1995). The insemination procedure is simple and takes about 5-10 min, usually being painless. It involves insertion of a speculum into the vagina to visualize the cervix. The cervix is then cleaned with a little culture medium. The washed sperm is then injected into the cavity of the womb using a fine plastic catheter. After insemination, the patient may be asked to rest for a short period of time (Ombelet *et al*., 1995). IUI is ideal in those cases where infertility is due to sexual dysfunction (impotence, retrograde ejaculation, etc.,) or due to timing issues. Sometimes the cervical mucus acts as a barrier to the activation and passage of sperm as it passes through the cervical canal. Such hostility may be due to poor physical qualities of the mucus, cervical infection, or the presence of antisperm antibodies. In all but the latter case, IUI can readily be performed during natural cycles, unless the woman has ovulation dysfunction (Ombelet *et al*., 1995). However, when infertility results from the presence of antibodies in the cervical mucus, IUI will likely be ineffective and should be replaced by IVF.

Gamete intrafallopian tube transfer: Gamete Intrafallopian Transfer (GIFT) is an ART procedure that was introduced in 1984 (Asch *et al*., 1985). It involves superovulation, egg retrieval from a woman's ovaries, mixing of retrieved eggs with washed and capacitated sperm and placing of the mixture into the woman's fallopian tube(s) through a small incision in her abdomen. The procedure is thus performed by laparoscopy. As one may easily notice, the procedure is practically the same as for IVF, the only differences being that fertilisation occurs *In vivo* (in the fallopian tube), rather than *In vitro* (in the Petri dish) and that laparoscopy is excluded in IVF. GIFT by-passes the picking up of eggs by the fallopian tubes and is hence ideal when there is reduced motility of the fimbrae of the fallopian tubes (Asch *et al*., 1985). Since eggs and sperm are placed directly into the ampullary

region of the fallopian tube, fertilization and early embryo development occur in the natural protective environment and the embryo is transported to and enters the uterine cavity in a physiologic manner. An ectopic pregnancy is one in which the embryo implants and starts developing in the fallopian tube rather than in the uterine cavity, a condition which can threaten one's life. GIFT does not increase the incidence of ectopic pregnancies, unless it is performed in damaged fallopian tubes (Sher *et al*., 1995). Hence, GIFT should not be performed if any damage of the tubes is suspected, even in those cases where surgery seems to have solved the problem. This is because there is no way of knowing whether the inner lining of the tubes are intact and if peristaltic movements are normal (Sher *et al*., 1995).

Zygote Intrafallopian Transfer (ZIFT) and tubal Embryo Transfer (ZET): Zygote intrafallopian transfer (ZIFT) and Tubal Embryo Transfer (TET) are techniques which combine IVF with GIFT in order to produce a pregnancy. Both procedures involve fertilization of eggs with sperm in the laboratory, as in IVF. Once these eggs have been fertilized, they can be transplanted into the fallopian tube by laparoscopy either at the zygote stage (ZIFT) or at the embryo stage (TET). The advantage that TET is thought to have over ZIFT is that it allows selection of the best quality embryos while at the same time giving the patient additional time for recovery from the egg retrieval (Berger *et al*., 1995). The zygote or embryo can then move down the fallopian tube and into the uterine cavity, where it is hoped that implantation will take place.

ZIFT/TET are not yet among the commonest procedures since they are considered to be among the most invasive types of fertility treatments available to infertile couples. As a result, ZIFT/TET accounts for only 1% of all ART procedures (Berger *et al*., 1995). ZIFT/TET is particularly indicated where the cause of infertility is male factor and is combined to difficult transcervical intrauterine transfers.

Intracytoplasmic sperm injection: Intracytoplasmic Sperm Injection (ICSI) involves the injection of a single sperm into a single egg in conjunction with IVF in order to get fertilization. ICSI is most commonly performed in those cases with severe male factor infertility i.e., sperm concentrations of less than 15-20 million per millilitre, sperm motility less than 35% or very poor sperm morphology (Holmann, 2002). The sperm preparation technique for ICSI is different from that performed in IVF; samples are usually oligospermic or asthenozoospermic and hence cannot be prepared by density centrifugation or swim-up techniques. The sample would first be centrifuged for 5 min, then washed with medium and then the pellet is resuspended in a small volume of medium. The sample is then directly applied to the injection dish, or an aliquot of the suspension is added to a drop of HEPES buffered medium. When possible, the injection pipette is used to select a moving sperm with normal morphology from this drop and is then transferred into a drop of Polyvinyl Pyrrolidine (PVP). PVP is a viscous solution used to impair sperm motility prior to immobilisation and aspiration into the injection pipette. Any debris that is attached to the sperm is cleaned by pipetting the sperm back and forth with the injection pipette (Elder and Dale, 2000).

During the injection procedure, the mature egg is held with a specialized holding pipette which aspirates the ovum gently thus attaching it to the pipette. It is important that the oocyte is positioned such that its polar body is at 6 or 12 o'clock, thereby minimising the possibility of damaging the meiotic spindle (Elder and Dale, 2000). The injection pipette which would have been previously used to immobilise and pick up a sperm is then carefully inserted through the zona pellucida and into the cytoplasm of the egg. The sperm is injected into the cytoplasm and the needle is then carefully removed. Finally, the eggs are transferred to a culture dish and left in the carbon dioxide incubator overnight and then checked the next morning for evidence of normal fertilization (Hafmann, 2002).

Ethical implications

Should research on surplus human embryos be permitted?: Although human embryo research is a purely scientific development, yet it involves human reproduction and transfer of genetic material. Many societies feel that they are not only concerned with what happens in this field, but they ought to monitor, watch carefully, regulate and even sometimes restrict or totally ban such development (Serour, 1992). Many believe that the human embryo is the beginning of human life due to the nature of its genetic material, DNA and the structure of its chromosomes (Seller, 1993). However, one must not forget that it is not only the human embryo that is genetically unique, but every sperm and ovum is also genetically unique. Furthermore, not every sperm cell and ovum or even an embryo develop into a human person. There is an enormous natural prenatal loss which is known to occur. Indeed, if everything is favourable, then a human being gradually emerges in only about 20% of embryos (Seller, 1993). It is therefore, not surprising that some ethists and scientists do not consider the first stages of the embryo as a human person and may, therefore, allow experiments on it which involves its

destruction (Seller, 1993). However, one must not neglect the potentiality of human embryos to develop into a human person. This means that great respect must always be accorded with it. Experiments which may harm the embryo, while still allowing it subsequently to realize its potential and become a person, should hence not be permitted (Seller, 1993).

ICSI: In spite of severely compromised semen characteristics ICSI enables fertilization to take place. However, due to the absence of natural selection of the fertilizing sperm and the oocyte to be fertilized, any structural damage caused by the operation, or transfer of genes that would not normally have been passed on to the child, ICSI could possibly increase the risk of developmental abnormalities and health problems in the children (Harris and Holm, 1998). This raises a series of moral issues. Can a possible increase in the risk of birth defects be accepted? and if yes, on what grounds can it be accepted? Moreover, is the increased risk accepted relative to the risks associated with normal birth, Oocyte Donation (OD), or adoption? Furthermore, what kind of birth defects can be accepted-congenital malformations, growth disturbances, neurological developmental disturbances, chromosomal abnormalities, or transmission of subfertility to male offspring? On the other h and, if this higher risk is not accepted, then what should implicitly be said about the value and worth of people that have these birth defects? Moreover, what moral responsibility should one have for those children born with birth defects and who has responsibility for taking care of them and paying the extra costs involved (Pandit, 1999). The point here is not to answer all these questions but rather to highlight the variety of moral issues related to the risks associated with ICSI. The answers to the questions depend on whether we are asking them to an infertile person, the couple, the child, the professional, or the public in general (Pandit, 1999). In contrast to traditional IVF, ICSI is in most cases treating one person for another person's condition: the woman is treated for the man's infertility. One could argue that it is not infertility *per se* that is the problem but rather not having children. As childlessness is a condition the couple has in common, treatment that involves both partners is legitimate (Robertson, 1996). This argument is controversial because single women and men, as well as homosexual couples, may also suffer from childlessness and thus should also be treated. However, societies often draw moral distinctions among these groups (Robertson, 1996).

CONCLUSION

The benefits of IVF are many, but unfortunately these are sometimes obscured by the ethical implications that it also gives rise to. Some view IVF as something which interferes with the natural way of living of humans whereas others think that IVF interferes with the laws of God or whatever other entity rules our world. Some think that IVF involves killing of embryos-that these are sacrificed in order to give birth to a baby. How can such mentalities be improved? The answer is education-proper information should be made available so as to make societies aware that the early stages of an embryo are not actually an embryo but only a group of cells and that any surplus pre-embryos can be frozen, thus avoiding their destruction whilst giving the couple the opportunity to have a second child or to donate them to other couples which can't produce embryos of their own. These issues are not to be viewed as an obstacle to advances in reproductive technologies, but rather as a means to provide a conscience to society, to keep the aims of such techniques honest and morally correct and to make sure that the beneficial outcomes of IVF outweigh the negative ones. Further research, with the goal of improving IVF and other ART techniques, should thus be encouraged. One cannot neglect the fact that the basic goal of techniques like IVF is to improve the quality of life of infertile couples and, as long as the health and happiness of children conceived through IVF is not affected, reproductive technologies should be praised and not condemned, because IVF certainly can change one's life forever.

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