Infertility Management: What's the Latest ?

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I. INTRODUCTION

The number of babies born due to infertility treatment with in vitro fertilization (IVF) worldwide is estimated to be more than 8 million since the birth of the world's first IVF baby 43 years ago. IVF and other fertility treatments may enable 400 million people or 3% of the entire world's population to be alive by the year 2100.

As a result of the rapid growth of novel technologies in reproductive endocrinology and infertility (REI), such as intra-cytoplasmic sperm injection, oocyte cryopreservation, preimplantation genetic manipulation of embryos, and embryonic stem cell biology, assisted reproductive technology (ART) is catalyzing a "renaissance", a period of vigorous artistic and intellectual discourse concerning these fields.

Over the past four decades, IVF technology has developed beyond the imagination. The purpose of this article is to briefly describe and summarize the many advances seen in reproductive medicine in recent years.

Male Infertility: Advances in Treatment

ICSI (Intracytoplasmic sperm injection)

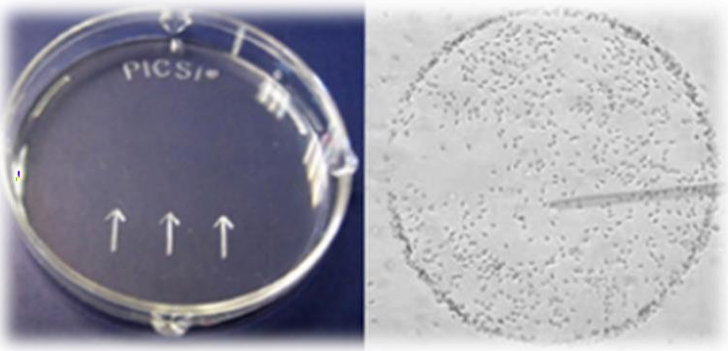
By injecting a single sperm into an ovary, couples with male factor infertility have been able to improve their fertility treatment outcomes, and in 1992, the first "ICSI baby" was born in Belgium.

The advent of ICSI has revolutionized assisted reproductive technology, enabling us to treat patients more efficiently with:

1. Oligoasthenoteratozoospermia
2. Testicular spermatozoa
3. Limited number of oocytes
4. Previous IVF failures

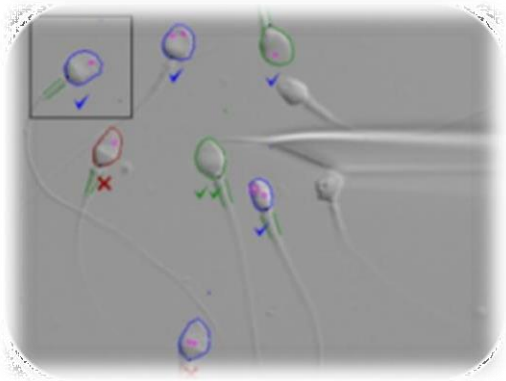
PICSI

In a physiological intracytoplasmic sperm injection (PICSI), sperm are selected before they are used in intracytoplasmic sperm injection (ICSI). In this procedure, the sperm is placed in a solution of hyaluronic acid (HA), a naturally occurring compound. A PICSI procedure identifies one sperm that is capable of binding to HA, and these sperm are chosen to be used in treatment. Even non-trained embryologists can recognize spermatozoa that have been bound by HA.



IMSI

A technique called IMSI, or Intracytoplasmic Injection of Morphologically Injected Sperm, consists of the injection of sperm from a male under very high magnification. This method has been shown to increase pregnancy rates and ICSI failure rates. When IVF is needed for male factor, unexplained infertility, and previous failed ICSI, the healthiest sperms are selected and are injected with the help of a machine. These sperms are then transferred into the eggs taken from the women. Moreover, it has been found to be effective in preventing recurrent abortions after IVF and ICSI procedures.



SURGICAL SPERM RETRIEVAL TECHNIQUES

In cases of azoospermia, the only hope is surgically removing the sperms from the testes or epididymis followed by ICSI.

When there is an obstruction (Obstructive azoospermia)

If sperm cells cannot be released because of an obstruction, there are four different techniques available for harvesting them. It is possible to perform three of these procedures under local anesthesia while the fourth is done under general anesthesia.

1. Testicular Sperm Aspiration (TESA)
2. A needle is used to withdraw sperm-containing fluid from the testicles.
3. Percutaneous Epididymal Sperm Aspiration (PESA)
4. As part of this procedure, a needle and syringe are also utilized to extract the sperm-containing fluid. The needle is, however, inserted into the epididymis in this case.
5. Percutaneous Biopsy of the Testis (Perc biopsy)
6. A larger needle is used to retrieve sperm in this method of sperm retrieval, which is similar to TESA. An area of testicular tissue is biopsied using a larger needle. This method allows for a greater amount of sperm to be obtained.
7. Microsurgical Epididymal Sperm Aspiration (MESA)
8. Operating microscopy is used during this open procedure in order to locate the tubules within the epididymis. Through this procedure, a large sample of sperm can be retrieved. In addition to producing large sperm samples, this procedure is also believed to produce motile sperm. IVF or ICSI techniques that use this technique likely achieve a greater success rate.

When there is No Obstruction (Non-obstructive azoospermia)

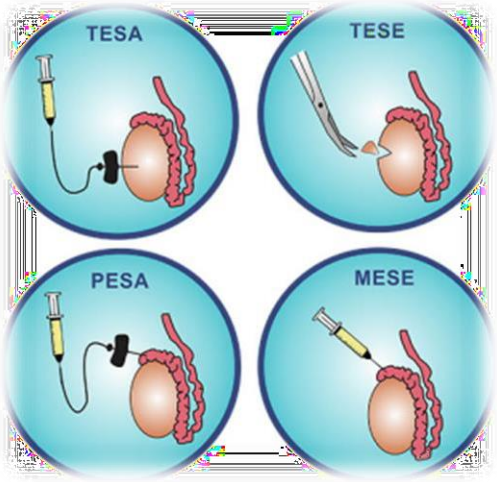
A man who has no obstruction in the vas deferens and whose sperm does not contain any sperm usually has difficulty producing sperm. When the quantity of sperm produced is relatively low, more invasive techniques are required to retrieve sperm. These techniques include:

- **Testicular Sperm Extraction (TESE)**

In this procedure, a needle is inserted into the scrotum and a small amount of testicular tissue is removed. This is usually taken from multiple parts of the testicles. The sperm are then identified by a microscope and isolated from the remaining tissue.

- **Microdissection TESE**

There are many similarities between this process and a TESE. The tissue that needs to be removed is located with the assistance of a micro-dissecting microscope. The objective is to limit damage to the testicles. As well, the procedure aims to reduce the risk of adverse effects, such as the possibility of cutting blood vessels, which might affect the blood supply. In addition, it is believed that it can increase the quantity of sperm retrieved.



Advances in Embryology

1. **Assisted Hatching**

Embryos must hatch out completely before they can implant. It is estimated that only 25-30% of embryos hatch under optimal in vitro conditions. The process of assisted hatching can be accomplished using several methods, including partial zona dissection (PZD), chemical opening through the use of acidic Tyrode's solution, and zona drilling. Laser systems have recently been developed as an excellent method for manipulating zones.

2. **IVM**

IVM involves the process of induced maturation of oocytes that have been collected at various stages during embryo development. Clinical sources provide immature oocytes that may develop into embryos and result in live births. Patients suffering from polycystic ovary syndrome (PCOS), ovarian hyperresponsiveness, or hyporesponsiveness may benefit from IVM treatments. Additionally, patients suffering from cancer may be able to preserve their fertility through IVM.

3. **Embryoscope/Time Lapse Embryo Monitoring**

An incubator with an integrated camera that captures pictures of developing embryos regularly is referred to as this type. An integrated camera system is connected to a microscope. Image-processing software is used to combine the captured images into a time-lapse video. An embryologist can thus assess the growth stages of an embryo and thus select the best without removing it from the incubator.

4. **Chromosomal Screening by Preimplantation Genetic Testing (PGT)**

PGT is a procedure used to detect genetic abnormalities in embryos developed through in vitro fertilization. The procedure is performed prior to embryo transfer to the uterus. In PGT, the objective is to minimize the likelihood that an embryo will transfer with a genetic abnormality or chromosome abnormality.

- **Preimplantation genetic testing for aneuploidy (PGT-A)**:

During PGT, embryos are screened for certain types of chromosome abnormalities, such as missing or extra chromosomes (aneuploidy).

- **Preimplantation genetic testing for monogenic disorders (PGT-M):**

Embryos that are subjected to this type of PGT are at increased risk of developing a specific genetic disorder. PGT-M is recommended when there is a genetic condition that could pass from one generation to the next, for women who are carriers of X-linked conditions, or when both an individual and their partner or donation are carriers of an autosomal recessive condition.

- **Preimplantation genetic testing for structural rearrangements (PGT-SR):**

A patient or their partner may require this type of PGT when they have a rearrangement of their chromosomes, such as translocation or an inversion.

- **Omics-**

Proteomics, metabolomics, and secrotomomics are among the omics technologies that have already demonstrated that viable embryos possess unique molecular profiles and potential biomarkers that may be useful for embryo selection.

- **Polarization Microscope(Poloscope)-**

Oocyte, embryo, and sperm quality can now be determined using this revolutionary tool.

Current Therapies to Improve Endometrial Receptivity

1. **Endometrial Scratching**

The process of endometrial scratching, which is also called endometrial injury, involves the intentional disruption of the endometrium with the purpose of increasing the likelihood of implantation. This is done before the planned cycle. More evidence is needed in its favor.

2. **G-CSF**

The use of G-CSF (granulocyte colony-stimulating factor) may increase the thickening of the endometrium in patients with abnormally thin endometrium when other methods to improve its thickness are insufficient.

3. **Platelet Rich Plasma (PRP)**

A new treatment method for thin endometrium that utilizes Platelet-Rich Plasma (PRP) is available. Plasma is centrifuged blood that contains a large number of platelets. In PRP, the patient's blood is used. It contains many growth factors and cytokines, such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor (TGF), and many others that support wound healing and tissue regeneration. Instilled intrauterine or subendometrially.

4. **Stem Cells**

It is possible to isolate endometrial angiogenic stem cells using immuno-magnetic isolation from autologous stem cells derived from the patient's bone marrow. Following curettage, these cells can be placed under ultrasound guidance in the endometrial cavity to help regenerate the endometrium.

Cryopreservation

The cryopreservation of oocytes and ovarian tissue holds promise as a technique to make fertility preservation easier and more accessible to a wider population.

Uterine transplantation

A uterus transplant begins with a donor's uterus being removed. This surgical procedure involves the transplantation of a healthy uterus into an individual whose uterus has been removed or is incurably ill. All women undergoing a uterus transplant are required to freeze their eggs prior to the procedure. After the procedure, the couple will have to wait a year before they can undergo in vitro fertilization. It is expected that fertilized eggs will be implanted one at a time to achieve pregnancy and that the women will undergo cesarean delivery to avoid overstressing the transplanted uterus. An organ transplant may be complicated by complications such as bleeding and infection for the recipients. During the period in which the uterus is implanted, the patients will receive anti-rejection medications. The uterus will be removed after giving birth.

Future Trends Mitochondrial Replacement Therapy (Three- Parent Baby)-

Using this technique, the cytoplasm of the egg/embryo is replaced completely, preventing the transmission of undesired mitochondrial defects in patients with inherited mitochondrial diseases.

- **Gene editing (CRISPR-CAS9)**

The process of gene editing involves inserting, deleting, modifying, or replacing DNA at a specific site to modify the genome.

- **Stem cells**

Stem cells are being considered for the treatment of premature gonadal failure in both males and females, diminished ovarian reserve as well as regenerating endometrium in cases of persistently thin endometrium.

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