

OUR CENTER

- HISTORY

THE FERTIVITRO

The Center for Human Reproduction — FERTIVITRO that was founded in March, 2001 has the goal to increase the number of success cases in the area of infertility treatments. The clinic has a professional staff that is constantly updating its knowledge. They have impeccable reputation and a profound understanding of the fertility area. Our staff offers the most modern treatments with all the technology currently available in the market, in addition to humanized attendance to patients. The center also offers financial aid to help many couples make their dream come true.

INFERTILITY CAUSES

- INTRODUCTION

Definition of conjugal infertility

It is the inability of a couple to become pregnant, after one year trying when having frequent sexual intercourse without contraceptive methods.

A couple with an active sexual life, that does not use contraceptives, has a one out of five chance to conceive each month (20%). That means that eight out of ten couples, when trying to have a baby, will get pregnant within a period of one year. However, the 20% present some difficulty in having babies through natural ways and, at least half of them will need to resort to assisted reproduction treatments.

Conjugal infertility affects 15% to 20% of couples in reproductive age.

Infertility Causes

The factors that cause infertility to a couple may have either feminine or masculine origins. We know that currently around 30% have feminine causes, 30% have masculine causes and 25% are from both men and woman.

However, around 15% of couples do not know the real cause of infertility, even after analysis's results of every exam performed. It is not possible to find a definite conclusion regarding the diagnosis of infertility. These cases are classified as Infertility or Sterility of no apparent cause (INAC or SNAC).

For women, the causes of infertility may be associated with the following factors:

Cervical factor (uterine cervix), uterine factor, tuboperitoneal factor and ovarian factor, immunological factor and age.

- MENSTRUAL CICL

To Understand the Menstrual Cycle

Every month, a woman's body prepares itself to get pregnant. In the ovaries there are follicles (rounded structures filled with liquid), where the eggs develop and mature.

To successfully complete the process it is necessary the production of many hormones like: FSH (Follicle-Stimulating Hormone) and LH (Luteinizing Hormone), both produced by the pituitary gland, and also estradiol, produced by the ovaries.

FSH and LH are responsible for the development of the egg; simultaneously, estradiol is produced by the ovaries, making the endometrium, layer that lines the uterus internally, thicker with the objective to prepare it for pregnancy.

Although there is the possibility that many follicles might grow, only one will reach a bigger size and will break at the moment of ovulation. The result in the majority of cases is that only one egg is released. LH is also the hormone that is responsible for the breaking of the follicle.

The sac that holds the egg is called a follicle. After it is broken and it has released the egg, it is then called corpus luteum and it will produce estradiol and progesterone hormones.

Progesterone is important for the maintenance of pregnancy.

Progesterone's function is to stimulate the developing and secretion of the endometrium glands. Both are important sources of nutrition during the first days of pregnancy.

The implanted embryo produces a hormone called hCG (Human Chorionic Gonadotrophin), that keeps the corpus luteum active for around three months, until the placenta is developed and begins to produce the necessary hormones for the pregnancy.

If there is no pregnancy, the corpus luteum will regress, and levels of estradiol and progesterone will diminish, as a consequence of the hormonal drop, the endometrium begins to shed, and consequently the cycle of menstruation begins.

This cycle is repeated every month, during the reproductive life of a woman, in case there is no conception.

- CERVICAL FACTOR

The cervical channel produces, during the period before ovulation, a transparent secretion very similar to egg whites, called cervical mucus. The cervical mucus is responsible for transportation and storage of sperm or spermatozoa in the feminine reproduction tract. Once the sperm are in contact with the cervical mucus, they will go through a phase of maturation, that is, they become mature so they can fertilize an egg.

To evaluate the cervical factor, an exam called Post Coital Test (PCT) is done. The test consists of collecting the cervical mucus and the vaginal secretion four to twelve hours after sexual intercourse, and analyzing the presence and activity of the sperm (sperm quantity and mobility). It is important to remember that the PCT can only be done in the presence of cervical mucus in the period before ovulation.

In exams that there are no sperm or only non moving sperm, it is possible to be facing an immunological or genetic factor, however, this diagnostic can only be confirmed by specific exams and after a detailed semen analysis (spermogram).

- UTERINE FACTOR

The uterus has an essential role in the reproductive process because it is responsible for transporting the sperm and it is inside it that implantation takes place (when the pre•embryo fixes itself in the uterus) and where the fetus develops.

Uterine alterations are formed inside the uterus per se, as well inside the endometrium.

Inside the uterus it is possible to find malformations (alterations in its embryonic development), tumors (myomas are the most frequent) and adhesions or synchiae, that alter the form of the uterine cavity.

Myomas are benign tumors of the uterine muscular tissue that modify the uterus architecture. They could lead to an obstruction of the uterine fallopian tube inducing the uterus to contract and occupy a space inside the uterine cavity and that makes the implantation and development of pregnancy harder. Women with myomas may present difficulties to get pregnant or have abortions of repetition. It is important to clarify that this condition leads to infertility in a minority of cases. All women who have myoma should be very well evaluated regarding the size and location of nodules.

Other anatomical conditions of the uterus can also make it harder to get pregnant. There are uteruses with the septum inside the cavity that reduces the available space for the development of a pregnancy. Others present an incomplete development, with a very small cavity. There are as well "duplicated" uteruses, which can, eventually, be too small to allow gestation. And, at last, there are alterations of the endometrium that do not allow the implantation of an embryo, like polyps that, according with size or location, should be removed. In the endometrium, there could be infectious alterations (caused by agents like chlamydia, mycoplasma, gonococcus, etc.) and polyps, which presence may obstruct or prevent the correct implantation of the pre•embryo.

Endometriosis, condition where a tissue that is similar to the endometrium grows outside of the uterus, can affect the ovaries, intestines and cause adhesions to the pelvis, which in some cases can jeopardize the permeability of the fallopian tubes, resulting in infertility. Some symptoms of endometriosis are: intense pain during menstruation and sexual intercourse and also constant pain in the pelvic region.

The following exams are performed to diagnose uterine factor: Transvaginal Ultrasound, Hysterosalpingography and Hysteroscopy.

- TUBOPERITONEAL FACTOR

In order to a woman get pregnant naturally, it is necessary a contact between the egg and the sperm, this happens inside the Fallopian tubes.

It is very important to evaluate the form and function of the Fallopian tubes. They are responsible for the collection of the egg, sperm transport, union of the gametes, as well as the transportation of the fertilized egg (pre•embryo) to the interior of the uterus cavity. It is necessary to identify the obstruction of the Fallopian tubes and lesions that could jeopardize its mobility and the collection of the egg.

The most frequent causes of lesions in the Fallopian tubes are inflammatory processes (salpingitis), caused by infections through agents like Chlamydia, Mycoplasma, Gonococcus and others. Among the non infectious, the most common is a lesion caused by endometriosis (presence of endometrial tissue outside of the uterine cavity) and the least common are lesions caused by surgeries that include patients that had tubal ligation.

According to the type of obstruction and the woman's age, different types of treatment can be suggested to treat infertility, like for example; fertilization in vitro, procedure where the permeability of the tubes is not anymore necessary, once the fertilization of the egg is done in a laboratory.

- OVARIAN FACTOR

The ovarian factor is evaluated basically by analyzing hormone levels processed during the menstrual cycle. On the third day of the cycle (the first day is the beginning of the menstrual flow), three hormones are analyzed: FSH, LH and estradiol.

These hormones are extremely important to analyze indirectly the ovaries reserve. Around the 20th day of the cycle, the hormones prolactin and progesterone are measured. Progesterone levels are measured again three days later. Progesterone is a very important hormone, because its presence in normal levels means that the ovulation was successful.

It is also necessary to do a Transvaginal Ultrasound around the 12th day of the cycle, because, in this phase, it is important to verify that there is the presence of a dominant follicle. In addition, an analysis of the endometrium pattern should be done, with all its peculiar characteristics in this phase of the cycle.

For women that do not menstruate regularly, it is necessary to measure the hormones FSH, LH, estradiol and prolactin on the 3rd day of the cycle because generally they are anovulatory (have no ovulation).

The WHO (World Health Organization) classifies anovulatory patients in the following groups:

Group I:

Patients that present a dysfunction in the hypothalamic•pituitary axis. When these glands produce little quantity of gonadotropins (FSH and LH) and the quantity is not enough to stimulate the ovaries.

Group II:

Patients that present an irregular discharge of gonadotropins (FSH and LH), however, the levels are within the normal range, but generally there is an alteration of the relation between the quantities of LH and FSH (LH release being higher than FSH). Within this group, there are patients with Polycystic Ovary Syndrome. This syndrome is characterized by having enlarged ovaries that contain small follicles measuring 8mm to 10mm of diameter and clinical manifestations of an increase of masculine hormones (androgens), like an increase of body hair and acne.

Group III:

Patients that present an increase of gonadotropin release (FSH and LH) and a steep decrease of estradiol hormone. This hormonal condition represents a probable ovaries failure, condition more common in patients that are over 45 years old, but it can also happen earlier.

- IMMUNOLOGICAL FACTOR

Pregnancy is a particular condition from the immunological point of view, due to the fact that the embryo has half of its characteristics derived from the father, which is a foreign organism.

For this reason a harmonious operation of the immune system is essential to the progress of a pregnancy, because it will recognize the embryo as "foreign" and at the same time, accept its growth until birth.

It is believed that there should be a recognition process of the embryo by the maternal immune system, avoiding the embryo destruction, as if it was a foreign agent, like a bacteria or a transplanted organ.

Sometimes, small alterations of the immune function, even though it does not lead to any type of problem outside of the gestational period, could jeopardize the success of a pregnancy.

There are many ways to evaluate the operation of the immune system in these cases, with different types of treatment.

Many theories have been proposed to explain the process in which the maternal organism does not reject the embryo. Among these theories there is the production of antibody blockers that protect the embryo and also the control and balance of the defense cells activities of the immune system.

- WOMAN'S AGE

One of the main factors that determine the reproductive success of a couple is a woman's age. Unlike men, that produce sperm throughout their life, women are already born with a limited amount of eggs, which will grow old along with them.

From the age of 35 years old, the quality of eggs begins to decline. The chances of a successful pregnancy after the age of 40 are smaller. Besides the difficulty to get pregnant, the rate of abortion is bigger due to chromosomal alterations in the embryo.

It is important to highlight that the success of a pregnancy in patients above 40 years old, even with the most advanced assisted reproduction treatments, are not very encouraging. Patients around that age, many times will only be able to get pregnant with donated eggs. For this reason, it is essential and advisable that in cases of couples with difficulty to get pregnant, a detailed investigation should be done preferably before the age of 35.

In conclusion, women have a productive life that is limited by age. It starts on puberty and ends on the beginning of menopause.

TYPES OF TREATMENTS

- INTRODUCTION

Fertivtro offers all types of treatments that are recommended for conjugal infertility, ranging from low to high complexity, as well as complementary techniques.

Low complexity:

- Programmed Coitus;
- Intrauterine Insemination (IUI).

High complexity:

- Conventional in vitro fertilization;
- Intracytoplasmic Sperm Injection (ICSI).

Complementary Techniques:

- Cryopreservation or freezing of pre-embryos
- Cryopreservation or freezing of eggs;
- Egg donation;
- Pre-Implantational Genetic Diagnosis (PGD).

Results :

- What are the real possibilities of success with assisted reproduction?

- LOW COMPLEXITY

- Programmed Coitus
- Intrauterine Artificial Insemination (IUI)

Programmed Coitus

It is a treatment recommended to couples when the woman's Fallopian tubes show no obstruction and the man has a normal spermogram, that is, his spermatozooids are of good quality and enough quantity. This method consists of programming sexual intercourse for the probable moment of ovulation.

Medication is prescribed to stimulate the ovaries to produce a small number of follicles. Follicular growth is monitored by ultrasound exams and when at least one follicle has reached a diameter of approximately 18 mm, a drug is administered that unleashes ovulation, and after 36 hours, or in the moment of ovulation, sexual intercourse is recommended.

Intrauterine Artificial Insemination (IUI)

Intrauterine artificial insemination is a simple procedure and it can be done in the doctor's office. It consists of depositing the semen, which was processed in a laboratory, inside the uterine cavity, by a catheter introduced in the cervical orifice. This technique has the objective to approximate the sperm to the egg, to eliminate obstacles and facilitate the path to the Fallopian tube, where fertilization occurs.

Semen is composed of seminal liquid and sperm, which during sexual intercourse are deposited in the vagina. The function of the seminal liquid is to provide energy to the sperm and help transport them until the vagina. After sexual intercourse, the liquid is eliminated and only sperm penetrate the uterus.

The uterus has an initial part that is called uterine colon, which makes the connection between the vagina and uterus per se. The uterine colon produces a secretion called cervical mucus, which during ovulation, helps the sperm to penetrate with more ease in the uterus. Production of cervical mucus is controlled by estrogen and it increases when close to ovulation, that is, the closer to the ovulation, more and of better quality cervical mucus will be produced.

Some alterations in the semen like: volume, amount, motility and morphology may incapacitate the sperm to penetrate and survive in the cervical mucus. Intrauterine insemination is a method that tries to overcome the obstacles described above.

Some reasons to have intrauterine insemination performed are:

- Idiopathic infertility or Sterility of no apparent cause (SNAC);
- hostile cervical mucus;
- mild endometriosis;
- mild masculine factor.

Success rates of pregnancy after treatment by intrauterine insemination range between 15% to 20% per try. It is recommended a maximum of three repetitions. The option of more conservative treatments should always be taken into consideration in situations where there is the possibility. In case the treatment fails, the ideal action is to plan the start of more complex treatments like Conventional In Vitro Fertilization or Intra Cytoplasmic Sperm Injection.

- HIGH COMPLEXITY

- Conventional In Vitro Fertilization (IVF)
- Intra Cytoplasmic Sperm Injection (ICSI)
- Criteria for the beginning of treatment
 1. Development of follicles
 2. Follicular Aspiration
 3. Semen collection
 4. Insemination and fertilization of eggs
 5. Pre-embryo development
 6. Transference of pre-embryos

Conventional In Vitro Fertilization (IVF):

Conventional In Vitro Fertilization is a procedure in which the fertilization of the gametes is performed in a laboratory. The prepared sperm will be placed close to the egg in an appropriate culture and in ideal temperature and humidity conditions. The fastest sperm that also have the best fertilization potential will migrate in the direction of the egg and only one of them should penetrate the egg.

Treatment recommendation:

- Lack or obstruction of fallopian tubes;
- Unsuccessful tubal reanastomosis (Tubal Ligation reversal)
- Severe Endometriosis;
- Moderate masculine factor;
- Prior treatments were unsuccessful;
- Ovarian failure (Egg donation Program).

Intra Cytoplasmic Sperm Injection (ICSI):

ICSI is one of the biggest revolutions in reproductive medicine. It consists of the introduction, through a micropipette attached to an inverted microscope, of a sole sperm into an egg. This technique offers a treatment for many couples that before would have to resort to the use of a semen bank, like in the case of men that have a very low quantity of sperm.

ICSI is a very efficient treatment of severe masculine infertility. The procedure allowed the beginning of research that had the goal to study directly gametes and embryos (Pre Implantation Genetic Diagnosis).

As time went by, new applications started to appear for ICSI, like the use of sperm from the epididymis and the testicle.

Criteria for technical selection to be chosen will be based on prior medical history, prior gestations, general health and the ability of the couple to produce the necessary gametes for the fertilization process.

Assisted fertilization program requires a complete cooperation from the couple in all phases that includes essentially, six main steps:

1. Development of follicles by the ovary;
2. Eggs aspiration (Follicular Aspiration);
3. Semen collection and seminal processing;
4. Insemination and fertilization of eggs;
5. Pre-embryo development;
6. Transfer of Pre-embryo to the uterus.

Criteria for the beginning of treatment:

It is important that a complete research about the sterility of the couple is concluded. In other words, a good diagnosis establishes the best treatment.

To start the program, the doctor should discuss and evaluate the clinical history of the patients, so that they will be offered all necessary guidelines to begin the ovarian stimulation protocol.

Bellow you will find a description of each step of the process:

1 - Development of follicles:

In order to have a good follicular development may, drugs that will help control the process will be administered. It is possible to utilize or not medication before the month of the beginning of treatment.

In most protocols, follicular development is initiated in the beginning of the menstrual flow, after a vaginal ultrasound, with the objective to evaluate the ovaries and the endometrium. If the ultrasound exam is within normal patterns, the second step is the stimulation phase per se, when hormones produced by the gonadotropin cells (FSH and LH), located in the pituitary gland, will stimulate the ovaries.

Even though normal ovulation might occur, these drugs are administered due to the fact that production of many eggs is necessary. This is very important because if there are a higher number of eggs, there is a higher chance of success, and it is possible to select the best pre-embryos to be transferred.

The medication utilized does not present a health risk. All hormones from the protocols performed by Fertiviro are natural. The only exception is the inhibitor (used during ovary stimulation), but it does not act directly in the ovary, but in the inhibition of natural hormones that stimulate the ovaries.

Countless studies published worldwide report that there isn't an increase of physical anomalies or congenital malformation rates in children that were born with the help of fertilization in vitro.

Dosage of the medication is customized and it should be adjusted accordingly to the response of the follicular development. Monitoring of the ovarian response to the medications is performed periodically, through ultrasound and, when necessary, through hormone measurements.

When follicles are considered mature (presence of at least three follicles, bigger than 18mm of average diameter, and present a uniform growth) it means that that is the proper moment to start a third medication, chorionic gonadotropin (hCG), that will help the egg to become completely mature and ready to go through the process of aspiration and fertilization.

2 - Follicular Aspiration:

Egg aspiration is performed 35 to 36 hours after the chorionic gonadotropin injection. Admission to the clinic will be in the morning of the day specified by the doctor. It is necessary to fast for eight hours before the procedure.

The procedure is always performed with the presence of an anesthesiologist in the room because it is necessary the use of medication that will cause a mild sedation.

Follicular aspiration is performed by the doctor with the help of an ultrasound machine where an attached needle will be guided until the ovary, so the follicular liquid can be aspirated. This liquid is taken to the laboratory where the eggs will be identified. As soon as the egg is found, an evaluation of the stage development of the egg is performed (so the ideal moment for insemination can be determined). Once classified regarding the stage in which the eggs are, they are transferred to a culture (nutritive solution) similar to the one produced by the Fallopian tube. The eggs are kept in an incubator with ideal temperature and humidity and an adequate gas mixture. These parameters are rigorously controlled during the whole procedure.

The next step is insemination, where the sperm will be placed close to the eggs so penetration of only one sperm inside the cytoplasm can occur (fertilization).

The eggs can be fertilized in the day of the aspiration, according to the procedure below or frozen for future use.

3 - Semen collection:

Men with normal spermogram:

It is asked to husbands to avoid ejaculations for two days prior to the egg collection. They will be informed of the probable day for semen collection.

Fertivtro advises patients to take a shower before semen collection procedure. They should carefully clean the penis, with special attention to the glans penis with retracted prepuce.

Collection should be done by masturbation. Patients should not worry about the delivery time. Fertivtro has sufficient time to prepare the semen and inseminate the eggs.

Men with lack of sperm cells in the semen:

Azoospermia or the total lack of sperm cells in the semen can be classified as the most severe form of male infertility. It affects approximately 15% to 20% of infertile men and 1% to 2% of the general male population.

Azoospermia can be divided in two types: obstructive and non-obstructive.

In the obstructive azoospermia, there is production of sperm cells, but an obstruction stops them from being part of the ejaculation. Men that are affected are not considered fertile even though they produce sperm. Causes may be: congenital bilateral absence of vas deferens, prior infections scars or the result of inguinal, transurethral and scrotal surgery (vasectomy).

In some cases, treatment may be done by seminal tract reconstructive surgery (for example, vasectomy reversal). Pregnancy rates after reconstruction vary from 27% to 56% and results depend on many factors, like the location and duration of the obstruction.

Non-obstructive azoospermia is associated with a failure of the testicle in producing sperm adequately. Its production may be severely compromised or even absent. Causes are: genetic and hormonal alterations, cryptorchidism, testicular torsion, medication for systemic diseases (including cancer), radiation and toxins.

In the case of obstructive azoospermia, sperm may be obtained from either the epididymis or testicles. With non obstructive azoospermia it is possible to collect sperm in some cases directly from the testicle. In both circumstances the use of alternative techniques to obtain sperm is necessary.

These alternative techniques were developed with the objective to obtain sperm directly from the epididymis or testicle. They are known by the acronyms PESA, MESA, TESA and TESE and can be defined as:

- PESA: Percutaneous Epididymal Sperm Aspiration.
- MESA: Microsurgical Epididymal Sperm Aspiration.
- TESA: Testicular Sperm Aspiration.
- TESE: Testicular Sperm Extraction.

It is important to highlight that, before the advent of ICSI, cases of irreversible obstructive azoospermia and non-obstructive azoospermia had to be treated with donated semen.

ICSI allowed azoospermic men, before considered sterile, to become parentes.

Seminal Processing

The collected semen, either by masturbation or by puncture of the epididymis or testicular biopsy, is taken to the laboratory where it will be analyzed so the best technique of preparation can be defined. It will be then processed. This phase is very important because it allows the separation of the seminal plasma from the sperm, concentrating and selecting the most mobile ones and with more fertilization potential. Selection takes approximately two hours, and the whole process is performed in aseptic conditions and with disposable and sterile materials that are especially produced for that purpose.

4 - Insemination and fertilization of eggs:

After a period of two to three hours of incubation, in a specific culture medium, the eggs should be inseminated. In conventional In Vitro Fertilization, the processed and selected sperm are placed in contact with the eggs. Only one sperm should cross the membranes that line the egg and finally penetrate it. With Intracytoplasmic Sperm Injection, only one sperm is injected inside the cytoplasm of the egg. Follow below the explanation of techniques mentioned above:

Fertilization is confirmed between 17 to 20 hours after insemination, when the presence of male and female pronucleus are observed (2PN).

5 - Pre-embryo development:

Embryonic cleavage or the cellular division of pre-embryos is observed after 24 hours of the fertilization confirmation.

There are many methods to classify pre-embryos, but most of them are based on symmetry (size) and in the number of cells, as well as in the fragmentation percentage. Acceptable pre-embryos are the ones with higher number of cells, consistent cell sizes and the absence or a maximum of 20% fragmentation. The option to extend cultivation time until later phases of the development in vitro (morula or blastocyst) is an option to select embryos with more potential of implantation, in cases that there are a big number of pre-embryos, avoiding the freezing of many embryos.

6 - Transference of pre-embryos:

Transference of pre-embryos may be performed during many phases of their development, usually from two to five days after the follicular aspiration, and the better developed ones are chosen.

It is an extremely simple procedure. The patient lies down in a gynecological position. Her bladder should be full (the orientation is to drink water one hour before the transference). A catheter of transference, holding no more than four pre-embryos is introduced in the uterus by the cervical orifice, a completely pain free procedure. Pre-embryos are placed approximately 0.59 inches from the uterus wall. It is advisable to rest for a period of 30 to 40 minutes.

The patient is then discharged and can start normal activities little by little. It is advisable to avoid heavy physical activities until after the pregnancy test.

Pregnancy may not be confirmed with total accuracy until after two weeks of the transference. During the waiting period, it is normal for a couple to get anxious, but, under no circumstance should the medication prescribed by the doctor be suspended.

According to the Code of Ethics of the Federal Council of Medicine no more than four pre-embryos can be transferred to the uterus. This rule is due to the statistical fact that a higher number of pre-embryos do not enhance the success rate of a pregnancy, but enhances the chance of a multiple gestation. Exceeding pre-embryos should be frozen so they can be used in future transfereces which increase the chances of the couple to conceive, without the need to utilize medication to induce a new ovulation. The freezing should be authorized by the couple.

- COMPLEMENTARY TECHNIQUES

- Pre-embryo freezing
- Egg Freezing
- Eggs donation
- Pre-Implantational Genetic Diagnosis (PGD)
- Reasons for cancelling

Pre-embryo freezing

Freezing allows the conservation of pre-embryos in a temperature of -320.8 F, in a liquid nitrogen tank. To use this technique it is important that the pre-embryo is of good quality, that is, that it can endure all phases of freezing.

The technique consists of substituting the water present in the cells cytoplasm for a cryoprotective solution to avoid formation of ice crystals that are harmful for the pre-embryo during freezing. Its development is temporarily blocked. This process has the objective to preserve, in the least traumatic way, all cellular structures.

At the moment of thawing, cryoprotectors are taken out in a gradual way while the culture medium occupies their spaces so the cells start to resume their metabolic activities.

The couple will be informed about the possibility of pre-embryos freezing in the day of the embryonic transference. There is a Term of Agreement that should be signed by patients to authorize the procedure.

Egg Freezing

This very innovative technique consists of freezing the eggs with the objective to preserve the female fertility, in liquid nitrogen, so they can be used in the future. It is a safe method that does not represent any risks to the patient or the baby.

The most efficient method to freeze eggs is vitrification in which the cryoprotective solution goes from liquid to solid without the formation of ice crystals that are very harmful to the cells and could cause irreversible damages. Up to 95% of vitrified eggs overcome this process in comparison to 50% or 60% when other techniques are used.

Eggs freezing is suggested in the following cases:

- Patients that want to postpone pregnancy, without the perspective of having children before the age of 35;
- Patients that will go through chemotherapy or radiation treatment for cancer;
- Patients that have a family history of early menopause;
- Patients that do not want to freeze embryos for philosophical, ethical or religious reasons;
- Patients that accept to donate part of their eggs to an egg bank to help other couples that can't have children.

Eggs donation

This treatment was established for women that are incapable of producing their own eggs or with a very low production. The donation of eggs (oocyte) is a treatment that requires medical advisement. The donation of eggs is also suggested to women with genetic diseases that do not present PGD (Pre-implantation Genetic Diagnosis) and therefore, could pass the disease to their children.

The success in the donation of eggs is in the age of the egg donor. Eggs in women with less than 35 years have shown to be more apt to pregnancy. ("Aging and Reproductive Potential in Women", Fitzgerald C., Yale Journal of Biology and Medicine ? 1998; "Effects of maternal age on oocyte developmental competence", Armstrong DT, Theriogenology • 2001).

The donation of eggs is a simple procedure. Donors are patients that are in the process of in vitro Fertilization and respond very well to the medications, with the possibility of getting a big number of eggs, and because of that, they accept to donate part of them. All potential donors are voluntaries and should be researched concerning genetic and sexually transmitted diseases.

While the egg donor is in a program of ovarian stimulation and egg collection, the receptor should be prepared for pregnancy. This is also done by administering hormones. In fact, she will get two feminine hormones • estrogen and progesterone • to simulate a normal pregnancy cycle, in which the lining of the uterus cavity (endometrium) gets thicker so the implantation of the fertilized egg can happen.

After being collected from the donor the eggs are fertilized with a sample of prepared semen from the male partner of the receptor. Two or three days after fertilization, the pre-embryos are transferred to the uterus; the remainder of eggs generally is frozen for a later use. Eggs donation has shown to be a successful assisted conception technique and it is considered the only treatment for women incapable of producing eggs. Success rates reach up to 50% of pregnancy in each treatment cycle.

Pre-Implantational Genetic Diagnosis (PGD)

This revolutionary technique is performed in cases where there is a strong possibility of genetic diseases being transmitted to the offspring. It is an early form of prenatal diagnosis and it has the goal to prevent genetic diseases before the gestation has been established.

After the Intracytoplasmic Sperm Injection (ICSI), pre-embryos are kept in culture for three days; when they then reach the stage of six to eight cells. By micromanipulation, one or two cells are taken from each pre-embryo that will be analyzed by molecular biology technology. Only pre-embryos that have no chance to develop analyzed genetic diseases are transferred to the maternal uterus. Success pregnancy rates are similar to In Vitro Fertilization.

Reasons for cancelling

There is only one reason to suspend the treatment cycle: when the patient has a bad response to the follicle production. Even with an increasing dose of medication, the ovary does not respond or respond insufficiently, producing a low amount of follicles with low hormonal response. The chance is minimized by a precise monitoring, performed in each cycle, adjusting the medication dose in a personalized way. If there is any possibility of the patient not having eggs, the cycle is cancelled.

- RESULTS

What are the real possibilities of success with assisted reproduction?

The chances of pregnancy per try reach up to 50% per treatment cycle. Global rates of successful assisted conception are higher than when done naturally. Because successes probabilities grow with each treatment cycle, it is possible to say that from each 100 couples that start an assisted conception treatment, after four cycles of treatment, this "accumulative" rate of pregnancy can go up to 80% per couple. The conception, however, is lower in women over 40 years old.

Pregnancy rate with the transference of four embryos and the age of a woman:

Woman's age	Pregnancy rate Clinic
< 35 years old	37,3%
35-39 years old	29,1%
40 years old or older	21,0%

Source: RLA 2000

PATIENTS GUIDE

- INTRODUCTION

The patients guide was elaborated with the objective to orient couples that will go through a infertility treatment. The idea is to show, in a simple manner, what couples that desire a pregnancy should know about the many techniques that are currently available.

After reading this guide, Fertiviro suggests patients to consult their doctors, if there are any doubts about the content presented. The clinic is also available to offer additional information.

Fertilization

A young couple that has regular sexual intercourse has one chance in five (20%) to conceive a baby every month. That means that eight in 10 couples (80%) that try to have a baby will get pregnant within a year. The other 20% are the ones classified as infertile.

The natural process to get pregnant is through sexual intercourse, where the semen is deposited in the back of the vagina. Semen is composed by male gametes sperm • and seminal fluid, that is responsible for transportation and also for providing energy to the gametes. After intercourse, only the sperm penetrates the uterus, while the seminal fluid is eliminated by the vagina.

The initial part of the uterus, called the cervix is the connection between the vagina and the uterus per se. It produces a secretion, the cervical mucus, that allows the penetration of sperm inside the cervix, during ovulation. The production of this mucus depends on estrogen • hormone that increases closer to ovulation • and makes the ideal quantity and quality, during the fertile period.

The fertilization then takes place in the fallopian tube, when the sperm (after crossing the vagina, uterus and fallopian tube) meet with the female egg.

In addition to the natural way, there is fertilization in vitro that takes place in a laboratory, when

the gametes are prepared and inseminated outside of the body. This is an assisted reproduction technique indicated when couples do not present favorable conditions for the natural fertilization inside the fallopian tubes.

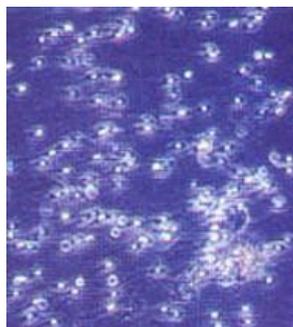
To better understand Assisted Reproduction Techniques (ART), Fertiviro presents below a summary of the main adopted treatments.

- DIAGNOSING THE PROBLEM

- [Semen Analysis](#)
- [Hysterosalpingography \(HSG\)](#)
- [Transvaginal Ultrasound \(TVUS\)](#)
- [Hormonal Measurements](#)
- [Progesterone Dosage](#)
- [Prolactin Dosage](#)

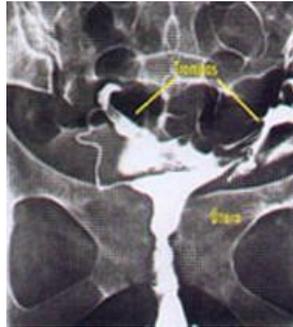
Semen Analysis

A sample of semen is collected in a sterile recipient and it is taken to the laboratory (see Picture). The best results are obtained after 2 to 3 days of sexual abstinence and when the sample arrives at the laboratory no longer than 30 minutes after ejaculation. Next the sample is evaluated in terms of volume, number of sperm cells, motility and morphology (form). Even though normal figures vary between laboratories, the World Health Organization (WHO) suggests a count of at least 20 million/ml, a directional motility equal or over 50% and the presence of at least 30% of oval sperm. This is the most important test to detect male infertility.



Hysterosalpingography (HSG)

It is an X-ray exam where a contrast is injected through the cervix inside the uterus and the fallopian tubes while the doctor observes the whole procedure in a video screen. (site picture). It should be performed at some time between the end of the menstrual period and ovulation.



In some patients, especially those with blocked Fallopian tubes, it could be somewhat uncomfortable. It is useful to determine if the Fallopian tubes are open and if the uterus cavity has a normal format.

Transvaginal Ultrasound (TVUS)

A transducer is inserted inside the vagina and that allows for the observation of the uterus (site picture) and of the ovaries through a monitor. This exam is performed to look for uterine abnormalities and ovarian cysts and to follow patients that use medication for fertility treatments and initial phase of pregnancy.



Hormonal Measurements

Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH) e Estradiol Hormone (E2).

A sample of blood is collected the closest possible to the third day of the menstrual cycle. FSH and LH are hormones produced by the pituitary gland and their levels are related to the ovarian functioning, increasing as the menopause gets closer.

Estradiol it is a response of the ovary to the stimulus of FSH and LH.

Progesterone Dosage

It is an exam performed, approximately, one week after the beginning of the menstrual period, because in a normal cycle this is the phase when the levels of progesterone peak. A good level of progesterone confirms ovulation. This exam may be used to monitor patients that use medications to treat infertility.

Prolactin Dosage

Ordered in most cases with Progesterone Dosage. The increase of prolactin may represent problems in ovulation and implantation (phase when the pre-embryo attaches itself to the uterus).

