



**gravida**  
fertilitat avança



# **In Vitro Fertilization (IVF / CSI)**

## What does it consist of?

In Vitro fertilization (IVF) is an assisted reproduction technique (ART) that consists of the fertilization of the oocyte (the female gamete) by the spermatozoon (the male gamete) in cultivated conditions in the laboratory, that is to say outside of the female reproductive system. Several steps must be taken to carry out this technique: ovulation is stimulated, an ovarian puncture to obtain oocytes is performed, a sperm sample is taken, the oocytes and sperm are put into contact, and the resulting embryos are cultivated to be placed later in the interior of the maternal uterus with the aim of achieving a pregnancy.

Since 1978 when Steptoe and Edwards published their work of having achieved the first child by way of conventional IVF, various related techniques have been developed, among these are IVF by Intra Cytoplasmic Sperm Injection, using isolated sperm cells obtained by testicular biopsy; assisted embryo hatching; and Preimplantation genetic diagnosis (PGD).

## ¿Cuándo está indicada?

### IVF for sterility:

- Tubal factor: absence, obstruction, or injury of the fallopian tubes
- Endometriosis
- Male factor (alteration of the concentration, motility, or morphology of sperm)
- Sterility of an unknown origin
- Failure of less intrusive treatments: stimulated ovulation, artificial insemination
- Diminished ovarian reserve
- Immunological disorders

### IVF in the absence of sterility:

- Preimplantation genetic diagnosis (PGD), with the objective of identifying and rejecting affected embryos
- Preservation of fertility
- Serodiscordant couples: couples in which one of the members suffers from a chronic, sexually transmitted disease which impedes natural gestation because of a risk of transmission

## Requirements of the couple

IVF cycles can be carried out in all women who meet the following requirements:

- The presence of a uterus capable of gestation
- Menstrual cycles
- The absence of a physical or mental maternal disease that contraindicates hormonal and/or gestational treatment

## Phases of the procedure

In a normal menstrual cycle, two phases can be distinguished: the follicular phase and the luteal phase, each separated by ovulation. In the first phase, generally one follicle is developed in one of the two ovaries where the future ovum is to be found. When carrying out an IVF cycle, we attempt to increase the number of follicles, oocytes, and embryos so as to increase the possibility of pregnancy.

### First phase: hormonal stimulation and monitoring.

Although the first pregnancies that resulted from IVF occurred in natural cycles (that is to say, without hormonal treatment), treatments involving stimulating ovulation were rapidly incorporated. This is done by administering gonadotropins with follicle-stimulating effects (FSH, LH, HMG). During this period a down-regulation of the pituitary function is usually provoked



with other pharmaceuticals similar to GnRH so as to avoid peaks of LH which would alter the maturing follicles. The majority of these medicines are commercialized in solutions to be applied subcutaneously, which facilitates self-administering. On this point, the function of the nursing staff to teach patients how to administer the doses is fundamental. The guideline for stimulation (the type of hormones and the dose) will be individualized and determined principally by age, ovarian reserve, the index of body mass, and the response to previous stimulations.

The process of stimulation will be monitored by a series of vaginal ultrasounds that permit us to study the number and size of the follicles, complemented by blood work to determine the hormone levels (basically estradiol).



The stimulation typically lasts 10 to 14 days depending on the protocol used and the response of each patient to the treatment. Once the optimum development of the follicle is achieved, the human chorionic gonadotropin (hCG) is administered so as to induce maturation of the oocytes, and a follicular puncture is programmed for 34-38 hours later.

## Second phase: Ovarian puncture

The follicular puncture is a simple surgical procedure carried out on an outpatient basis with local or general anesthesia of short duration (intravenous sedation) after which the patient will remain under observation for a period that varies from 2 to 4 hours. The follicles are located by ultrasound, undergo fine needle aspiration, and are submitted to the laboratory where the embryos are identified and the oocytes classified.



After this initial evaluation, the oocytes will be distributed in culture plates, duly identified and kept in an incubator for 3-4 hours prior to insemination or ICSI. At the same time, the couple brings in a sample of semen which will be treated and from which the best sperm will be selected by way of a wash and centrifugation to concentrate the most motile.

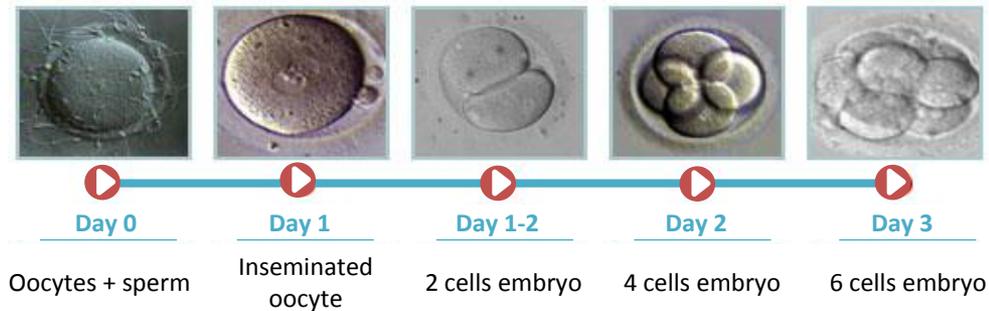


### Third phase: the fertilization of the oocytes

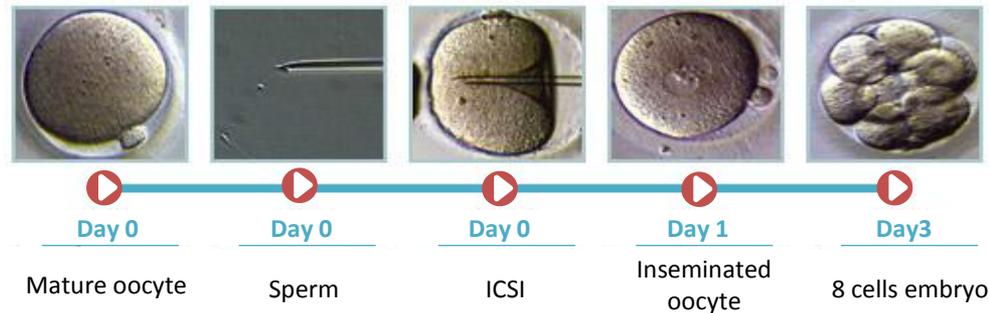
There are two techniques to place the oocytes into contact with the sperm: conventional insemination (which consists of placing some 100,000 sperm of good motility into contact with an oocyte, producing a natural selection of the sperm), or microinjecting a single sperm of good motility into each mature oocyte (ICSI). The use of one or the other fertilization technique is determined by the quality of the semen.

Regardless of the method employed, the inseminated oocyte will be kept in an incubator, the environment of which is controlled for temperature, humidity, and conditions of CO<sub>2</sub> y O<sub>2</sub>. The day after insemination, the oocytes will be tested to determine if they have been fertilized. After fertilization, cell division begins, giving rise to embryos, which will be evaluated and cared for in a laboratory so as to subsequently select those with the best potential for implantation.

*Sequence of conventional IVF*



*Sequence of IVF-ICSI*



#### Fourth phase: the embryo transfer

Finally, we proceed to the transfer of the embryos to the maternal uterus by way of the vagina. The embryo transfer is performed on the 2nd-3rd or 5th-6th day after the follicular puncture, selecting the best embryo(s). In young patients and with embryos of good quality, the most recommendable course is to transfer one or two embryos on the first attempts. In this way, the risk of multiple pregnancies is reduced, although the law 14/2006 of May 26 permits the transfer of up to a maximum of 3 embryos. The embryos are deposited in the uterine cavity monitored by ultrasound. It is an out-patient procedure that requires no anesthesia or hospital stay. With the aim of fostering the embryo transfer and good endometrial conditions, a hormonal treatment of progesterone is prescribed after the follicular puncture and will be maintained until the result of the cycle is known. Strict bed rest is not necessary after this procedure, though it is recommended that the patient refrain from strenuous physical exercise. 14 days after the embryo transfer a pregnancy test can be performed to determine if gestation has commenced. Confirmation of a pregnancy by way of an ultrasound will be carried out 15 days after the pregnancy test.

#### Fifth phase: cryopreservation

If once the embryo transfer has been performed, there remain embryos of good quality, these will be frozen in liquid nitrogen, so that the couple can use them in the future. Nevertheless, law 14/2006 of May 26 authorizes other possible uses: donation for reproduction, donation for scientific investigation, or ending their preservation.



#### Risks

**Multiple pregnancies:** The risk of multiple pregnancies is 20 to 25% and is related to the age of the woman, the number of embryos transferred and their quality.

**Ovarian hyperstimulation syndrome:** On occasion, the ovarian response to treatment is excessive, a large number of follicles are developed, ovarian size is increased, and the quantity of estradiol in the blood is elevated considerably. It is classified as light, moderate, and severe, the latter being rare (less than 2% of cases).

Other risks and complications that can exceptionally be produced:

- Adverse reactions or intolerance to the medication
- Complications of the follicular puncture (hemorrhages), although these are rare
- Cancellation of the ovarian stimulation due to inadequate or the absence of follicular development or an excessive response to the treatments
- Failure to obtain ova during the puncture
- Failure to carry out the transfer



## Results

The rate of success of IVF has been increasing in recent years thanks to scientific advances and improved laboratory conditions, offering a greater possibility of gestation. There are a number of factors that condition the probability and which are associated with each case: the cause of sterility, the number of embryos of good quality, and the age of the patient among others. Nevertheless, it must be remembered that not all patients who begin treatment achieve a follicular development sufficient enough to warrant puncture, nor do all patients who undergo ovarian puncture reach a successful transfer of embryos, given that in some cases there is a failure to obtain oocytes in the fertilization or during the embryonic development.

The record of IVF /ICSI of the Spanish Society of Fertility in 2005 lists rates of pregnancy as 30.1% for each cycle initiated, 33.9% for each puncture performed, and 38.1% for each embryo transfer.

80% of the pregnancies are achieved in the first three cycles of IVF/ICSI with satisfactory embryo transfers.

### **Gravida Fertilitat Avançada**

Av. Diagonal 660, Pl 16 Hosp. de Barcelona 08034

Barcelona

Tel: +34 93 206 64 89 - Fax: +34 93 205 76 86

[gravida@gravidabcn.com](mailto:gravida@gravidabcn.com)

*Together we can find the best solution*

