



REPRODUCTIVE
SCIENCE
CENTER of NJ

In - Vitro Fertilization Handbook

In Vitro Fertilization

Assisted Reproductive Technologies are used when a couple cannot be treated using simpler methods or the other methods have failed. These procedures have excellent success rates but require significant amount of effort, time and in some cases out-of-pocket expense. This can induce additional stress on a woman / couple. Our team helps to minimize these stresses by explaining the process fully and giving ample time for answering questions. Understanding the process helps you accept what is required to for this type of therapy to be successful.

Over the past decade, our knowledge and technological advances have increased the number of procedures designed to assist infertile couples in achieving pregnancy. The original and most often used infertility therapy is In Vitro Fertilization (IVF), which, along with other techniques, has substantially increased the likelihood of couples to have babies. The Reproductive Science Center offers all of the advanced reproductive technologies available worldwide. Some of these techniques will be briefly explained below.

Who is a candidate for in vitro fertilization?

Traditionally IVF has been offered to women with blocked, diseased or absent fallopian tubes. Currently IVF is offered to couples with a variety of infertility disorders who have not responded to conventional treatment. Some of these conditions include endometriosis, cervical mucus problems, male infertility, unexplained infertility and immunologic infertility.

All couples who wish to be considered for IVF must have an initial consult with the physician. Your prior clinical history will be reviewed to determine whether IVF is a suitable option. It is important that your medical records be made available at the time of this consultation. Your physician may request that certain fertility tests be performed before entering the IVF program. Also, other therapeutic options may be discussed at that time. If you would like to be considered for IVF, please schedule an appointment. We prefer that **both partners** be present at the time of the initial consultation.

Chances for success

The overall national delivery rate per egg retrieval is made available on the Internet by the Center for Disease Control (CDC) at www.cdc.gov/nccdphp/drh/arts/index.htm. The specific chance of success varies with a number of factors including the indication for the procedure, the patient's age, the number of embryos transferred and a variety of other factors. Your chances of success with IVF will be discussed on an individual basis with your physician. The success rate with IVF must be viewed considering the normal fertility rate in fertile couples that is approximately 20% per month.

The IVF Process

In Vitro Fertilization (IVF) is utilized for the more severe infertility cases involving severe endometriosis, pelvic adhesions, or problems that cannot be corrected with other treatments. The IVF process is complex and consists of several steps;

Ovulation Induction

Hormone injections are given to stimulate multiple egg production. This stimulation process usually begins with medication to synchronize the ovaries. Depending on your treatment protocol, Lupron, Ganerilix, or Cetrotide may be used to suppress the ovary and prevent ovulation. Daily gonadotropin injections are then added to stimulate the development of the eggs. These are usually given subcutaneously (under the skin) and are much less uncomfortable than the previous generations of medication. We then monitor the progress of ovulation induction with ultrasounds and blood estrogen levels over several days. Once the follicles are mature you will be schedule for an Egg

Egg Retrieval

On the day of the egg retrieval you will meet with the anesthesiologist who will interview you. You will be escorted into a holding room where an intravenous (I.V.) catheter will be started. During the procedure, medication will be administered through the I.V. in order to provide sedation.

The egg retrieval process is performed by placing a special needle into the ovarian follicle and removing the fluid that contains the egg. This is a relatively minor procedure and is performed by visualizing the follicles with a vaginal ultrasound probe. A needle is directed alongside the probe, through the vaginal wall, and into the ovary. To avoid any discomfort, strong, short acting intravenous sedation is provided.

Fertilization of the eggs and Embryo Culture

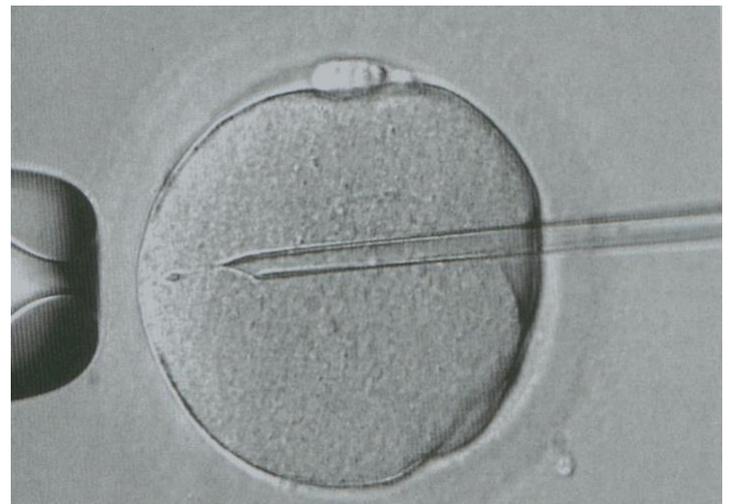
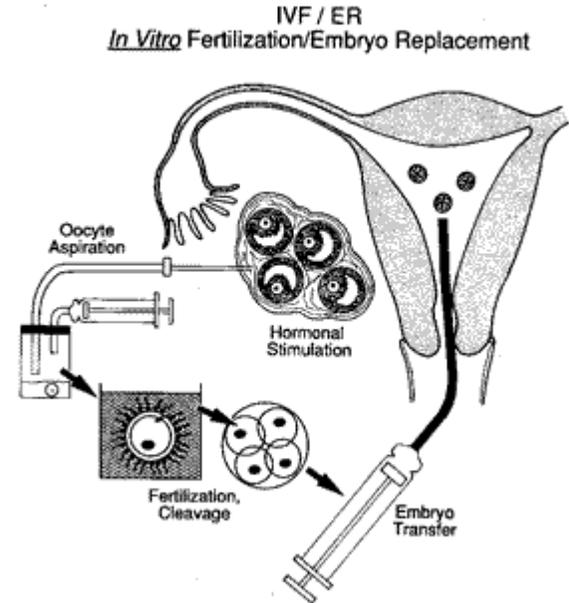
Once the follicular fluid is removed from the follicle, the eggs are identified by the embryologist and placed into an incubator. The eggs are fertilized with sperm later that day by conventional insemination or by Intracytoplasmic Sperm Injection (ICSI).

During conventional insemination approximately 50,000 sperm are placed with each egg in a culture dish and left together overnight to undergo the fertilization process.

The ICSI technique is used to fertilize mature eggs in the event of sperm or egg abnormalities. Under the microscope, the embryologist picks up a single sperm and injects it directly into the cytoplasm of the egg using a small glass needle.

ICSI allows couples with very low sperm counts or poor quality sperm to achieve fertilization and pregnancy rates equal to traditional IVF. It is also recommended for couples who have not achieved fertilization in prior IVF attempts.

The eggs will be checked the following day to document fertilization and again the next day to evaluate for early cell division. After fertilization they are called embryos and are placed in a solution called media to



Intracytoplasmic sperm injection (ICSI)

promote growth. Embryos are routinely cultured for three to five days and then transferred to the uterus and/or cryopreserved (frozen). Transferring a day 5 embryo, or a blastocyst, offers a lower risk of multiple births while providing a high chance of pregnancy.

On day two or three after fertilization, the embryos will be evaluated for blastocyst culture. If there is a sufficient number of dividing embryos they will be placed in special blastocyst media and grown for two or three additional days.

Embryo Transfer

Embryos may be transferred on day 3 or 5 after egg retrieval. Transfer performed on day 5 is called a Blastocyst Transfer. They are placed through the cervix into the uterine cavity using a small, soft catheter. This procedure usually requires no anesthesia. An ultrasound is performed while the catheter is being placed.

After the Embryo Transfer

After the transfer we recommend 48 hours of bed rest followed by 5 days of light activity. Progesterone is routinely given to support the uterine lining and could be given by an injection or vaginal application. This is continued until 10 - 12 weeks of pregnancy. At that time the placenta should be competent to make its own progesterone to maintain the pregnancy. In those patients who did not have an optimal response or if the embryology is poor we give estrogen in a pill form to enhance implantation. A blood test is performed 12 days after the embryo transfer to confirm a pregnancy.

Embryo Cryopreservation

Any excess high quality embryos resulting from the IVF cycle have the capability to be cryopreserved, or frozen, for future use. These embryos can be stored for a long period of time. You will be given a consent form for cryopreservation, which must be read carefully, signed and returned, prior to beginning your IVF cycle.

The embryos are slowly frozen using an extremely cold liquid (Nitrogen) and stored in holding tanks at the Reproductive Science Center of New Jersey..

IVF Embryo Quality

Embryo Grading

The grading of embryos has two purposes; first is to determine the number of embryos that should be transferred to avoid a multiple pregnancy and second to decide if the remaining embryos are of good enough quality for cryopreservation. The quality of an embryo is determined by assessing 3 major components; cell number, cell regularity (regularity of size), and degree of fragmentation.

The determination of "quality" is not made until about 48 hours after the egg retrieval. By 48 hours good quality embryos should be at least 4 cells. If they are not at least 2 cells by then, they are considered

"arrested" and should not be transferred. By 72 hours, 3 days after retrieval, we prefer that some of the embryos are at least 6 - 7 cells.

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The embryo transfer is an important variable that could affect the implantation process. The grades of the embryos have no relationship to birth defects, intelligence, strength, or athletic ability. The only difference as far as we know is in the chance that the transfer of the embryo(s) will result in a pregnancy and a live birth.

Additional Advanced Technologies

Assisted Hatching

Assisted hatching is a procedure in where the shell of the embryo (zona pellucida) is opened using micromanipulation. This helps the embryo shed its outer coating and in certain cases improves implantation and pregnancy rates. Assisted hatching has been shown to be beneficial in older women where the shell tends to be thick and in women who have tried IVF but were unsuccessful. Several studies have reported an increased pregnancy rate from 19% to 44%

The opening in the shell is performed using a chemical or laser technology. A small opening, between 10 to 20 microns, is made to facilitate embryo hatching. This procedure is very quick and can be completed in less than a half a second.

Blastocyst Transfer

With a natural conception the embryos arrive in the uterus approximately 5-6 days after fertilization in the fallopian tube. Recently, the laboratory techniques have improved to allow us to mature the embryos further. This has enabled us to select the embryos which have the best chance for survival.

By growing embryos to a more advanced stage we are able to transfer fewer embryos without decreasing the chance for pregnancy. This advancement maintains a high pregnancy rate while decreasing the risk of conceiving a high order multiple pregnancies.

Preimplantation Genetic Testing (PGT):

PGT allows detection of life-altering genetic abnormalities prior to embryo transfer. This technique reduces the number of women requiring chorionic villus sampling or amniocentesis. After the embryo is fertilized and allowed to grow, an embryo biopsy is performed. The embryos are cryopreserved awaiting the result.

As a woman gets older the chromosomes in the egg do not divide normally, therefore it is possible that too many chromosomes are present in the embryo, which could cause birth defects, pregnancy loss, and / or mental retardation; ex. Down's syndrome is due to an extra chromosome 21. Knowing whether the embryo is chromosomally normal can be completed within 24 hours, thus saving the parents undo stress for 9 months.

There is considerable need for chromosomal analysis of preimplantation embryos in couples carrying a chromosomal problem (ex. balanced translocations), in women with advanced age and women with previous children having genetic anomalies. Couples / women having recurrent pregnancy loss, repeated IVF failures or repeated poor quality embryos could also benefit from the PGD procedure to select healthy competent embryo.