

The ABC's of In-Vitro Fertilization

by Anita Singh, M.D.

Infertility affects one in twelve couples of reproductive age and is defined as the inability to conceive after one year of unprotected intercourse when the female is less than 35 years old, or 6 months if she is over 35 years old.

There are many causes of infertility. Approximately, 40 percent of infertility is related to female factors, 40 percent is due to male factors, 10 percent combined male and female factors and 10 percent unexplained. Many successful treatment options are available for the management of infertility. A consultation with a Reproductive Endocrinologist and an Infertility Specialist can help to identify the cause of infertility and the best available treatment options.

WHAT IS IN VITRO FERTILIZATION?

In Vitro Fertilization (IVF) is one of the many available options for infertility and is the process by which eggs (oocytes) are retrieved from the ovary, fertilized by the sperm in the laboratory and cultured into early embryos. The embryos are then transferred into the uterus. IVF is the treatment of choice in cases of infertility where both fallopian tubes are blocked. However, IVF may also be used as an option for those with unexplained infertility, endometriosis, cervical factor infertility, ovulation disorders, or when a man has a low sperm count. In fact, IVF has the highest per cycle success rate of all the available fertility treatment methodologies.



FERTILIZATION FACTS

The first baby from IVF was born in 1978. In data provided from the Centers for Disease Control (CDC) for the year 2003; 74,297 fresh, non-donor IVF cycles with embryo transfer were performed in the United States resulting in 25,775 live-birth deliveries. This corresponds to a 34.7 percent live birth rate per transfer. The per-cycle success rate with IVF is affected by many variables, the most important of which is the age of the female. In the 2003 CDC data, the live birth rate per transfer was 42.1 percent for women under 35 years old and declined with advancing maternal age to 6 percent for women older than 42. In order to put cycle success rates into proper perspective, it is important to understand that the normal monthly cycle conception rate for fertile couples is 20 percent. The monthly cycle conception rate for infertile couples with no fertility treatment is less than 10 percent.

HOW DOES IT WORK?

The IVF process involves a team of doctors, laboratory personnel and nursing staff working together to optimize the best possible outcome for the patient. Listed below are the steps in the IVF process:

1. Superovulation. The woman is prescribed self injectable fertility drugs for 8 to 12 days that stimulate her ovaries to grow more than one egg-bearing follicle. Fertility drugs are utilized because without them, only a single egg-bearing follicle would grow. This ovarian stimulation phase is monitored with periodic office visits for vaginal ultrasounds and blood tests. When these diagnostic methods indicate that the time is appropriate, an hCG (“trigger”) injection is taken to mature the eggs.

2. Egg Retrieval. Thirty-four to thirty-eight hours after the hCG injection, the eggs are retrieved from the egg-bearing follicles in the ovaries using ultrasound guided needle aspiration through the vagina. The follicles look like dark beads on the ultrasound screen. Intravenous anesthesia is administered for the procedure. The procedure usually takes 15 to 30 minutes. Depending on many factors, on average 8 to 12 eggs are collected. The eggs are aspirated into a test tube which is then examined by the IVF laboratory embryologist. The embryologist will determine the number of eggs obtained and classify them as mature, immature, post-mature or degenerative.

3. Semen Collection. The male partner’s prior sperm analysis determines the procedure the IVF laboratory team will utilize for inseminating the retrieved eggs. A fresh semen sample is collected and provided to the IVF laboratory team the day of the egg retrieval.

4. Fertilization. The semen sample is then processed in the IVF laboratory. One of two methods is used to inseminate the eggs with sperm. In standard insemination, a prescribed quantity of sperm is added – usually 100,000 sperm per milliliter – to a Petri dish containing eggs, and they “swim” together. In ICSI, which stands for Intracytoplasmic Sperm

Injection, a single sperm is injected into the cytoplasm of an egg. Over the next 18 hours, fertilization occurs in-vitro (in the laboratory). A fertilized egg has a single cell with two pronuclei, one from the mother and one from the father. When these two pronuclei fuse, they combine to create an original genetic package: an embryo.

5. Incubated Embryo Growth. Embryos are then cultured in the laboratory for 3 to 5 days before being replaced back into the uterus by a simple technique much like intrauterine insemination.

6. Embryo Transfer. The embryo transfer is usually done 2 to 5 days following egg retrieval. The majority of transfers are done on day 3 when the embryo is 6 to 8 cells. When a day 5 transfer is performed the embryo is more than 100 cells and is known as a blastocyst. The embryo transfer involves loading a thin catheter with the embryos and then gently placing this catheter under ultrasound guidance through the cervix and into the uterine cavity. Generally, 2 to 3 embryos are transferred back into the uterus depending on the patient’s age, embryo quality and physician recommendation.

7. The Wait. This is undeniably the hardest part – waiting 12 to 14 days before blood tests confirm pregnancy has begun. But, as many thousands of happy couples can attest, the frustration and unknowing associated with in-vitro fertilization very often results in the birth of a healthy child. The patient usually receives progesterone to support implantation and embryo growth during this phase.

SUPPLEMENTAL TREATMENTS FOR IVF

The IVF process may be supplemented with additional procedures as indicated. These additional procedures include:

1. Embryo Cryopreservation: In some IVF cycles more embryos are created than are transferred into the uterus. These excess embryos can be frozen (cryopreserved) for future attempts at pregnancy. In the United States in 2003, 17,517 frozen, non-donor embryo transfer cycles were performed per the CDC data. The live-birth rate per transfer for frozen embryos was 27 percent.

2. Assisted Hatching: A specialized IVF laboratory procedure that involves making a small “window” in the wall of the zona pellucida (outer shell surrounding the embryo), using a dilute, or weak solution of acid that is placed onto the surface of the embryo using a fine needle. The embryos are then transferred into the uterine cavity. Assisted hatching benefits women 38 years or older. It is also used in women who have failed multiple IVF cycles, in cases where embryo quality is poor, in some women suffering from endometriosis and in women with an elevated FSH level on day 3 of their cycle.

3. Pre-implantation Genetic Diagnosis: Pre-implantation genetic diagnosis (PGD) is the ability to screen embryos for specific genetic diseases before they are placed into the uterus. Transferring “screened embryos” lacking the genetic

defect of concern makes it extremely unlikely that the genetic disease will be passed to the child. PGD involves the removal of cells from a day 3 embryo, specialized genetic testing of this cell, with results obtained in about 24 hours, and then transferring into the uterus (or freezing) the embryos found to be normal.

4. Sperm Aspiration Procedures: These procedures known as testicular or epididymal sperm aspiration are utilized to obtain sperm for IVF from men that have no sperm in their ejaculate. One example is a man that has had a vasectomy. Another is a man with cystic fibrosis and congenital absence of the vas deferens. The aspiration procedure is a minor surgical outpatient procedure with sperm directly retrieved from the testis or epididymis. The aspirated sperm is then combined with the IVF retrieved eggs utilizing the ICSI technique.

5. Egg (Oocyte) Donation: Oocyte donation allows women who cannot conceive with their own eggs to become pregnant. The first successful pregnancy and delivery from oocyte donation was reported in 1984 from a woman that had premature ovarian failure. The source of donated eggs can be an anonymous or known donor. The egg donors undergo

ovarian stimulation with fertility medications and egg retrieval for the sole purpose of donating their eggs to an infertile couple. Once the donated eggs are retrieved they are fertilized in-vitro with the recipient partner's sperm. All the resulting embryos are then available for the recipient couple's use. Usually, two embryos are transferred into the recipients' uterus and excess embryos are cryopreserved for later use.

The IVF process can seem like a daunting one. However, understanding what is involved can help to ease some of the stress involved. IVF has come a long way since that first birth in 1978, and has allowed many couples who would have otherwise been childless to realize their dreams of parenthood.



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