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Infertility • Reproductive Endocrinology

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IN VITRO FERTILIZATION (IVF)

What is IVF? In vitro fertilization (IVF) is the original procedure among the *Assisted Reproductive Technologies* (ART). IVF is sometimes called “the test-tube baby” procedure. In the IVF procedure, a woman is given fertility medications to stimulate several eggs (8-10 or more) to develop in her ovaries. These eggs are then recovered from the ovaries through a procedure called transvaginal ultrasound egg retrieval. The eggs and the sperm from the husband are combined in the laboratory for 3-6 days, and then 2 of the healthiest embryos are transferred back into the uterus through the cervix in a procedure similar to intrauterine insemination (IUI).

How does IVF increase the chance of successful pregnancy? IVF appears to increase the chance of pregnancy in several ways. When several eggs are stimulated to develop in the ovaries instead of just one, the odds of pregnancy are improved. In addition, mixing of the sperm and eggs together in the IVF laboratory insures that adequate contact of sperm and eggs will occur and overcomes mechanical problems of tubal pick-up of the egg. Fertilization of the eggs in a Petri dish in the IVF laboratory requires a smaller number of sperm and is recognized as the best treatment for the majority of male (sperm) fertility problems. Finally, the use of fertility drugs may improve the hormonal environment for fertilization and early embryo growth.

How successful is IVF? The success rate (rate of live births) for IVF procedures at most centers for women less than age 40 is 35-45% per cycle when 2 embryos are transferred into the uterus. As with any of the ART procedures for the treatment of infertility, IVF can be an emotionally challenging process. In addition, the high level technology involved makes this type of treatment expensive. However, for certain types of infertility, IVF is a highly successful technique for the attempted achievement of pregnancy.

How is IVF done? The first step in the IVF procedure is ovulation induction. Instead of using a naturally occurring cycle, ovulation is induced with ovulation-stimulating or fertility medications. Ovulation induction for IVF results in the production of several eggs at the same time by the ovaries. The chance of pregnancy with IVF is maximized when at least 2 embryos are transferred into the uterus on day 3-6 after retrieval.

Ovulation induction usually begins with the use of a LUPRON injection each evening beginning after 7-10 days on birth control pills. LUPRON is used to temporarily suppress or block a woman's own signals to her ovaries and allows more mature eggs to be produced at the same time. After two weeks on this medication, an ultrasound exam of the ovaries and a blood test for estrogen are performed. A second injectable medication called FSH (GONAL-F or FOLLISTIM) and/or HMG (PERGONAL or REPRONEX) is then begun to stimulate the ovaries. After 4-5 days of these injections, vaginal ultrasound examinations and estrogen blood tests are performed every one to two days. After an average of five ultrasound examinations, the physician will know how many follicles (fluid-filled spaces within the ovaries which contain developing eggs) are growing and what size they are. The size of the follicles and estrogen blood test results are used to indicate when the eggs are ready for retrieval from the ovaries.

When the eggs are mature, an injection of a hormone called Human Chorionic Gonadotropin (HCG) is given. HCG causes eggs to finish the final maturation process and to be ready for removal from the ovaries approximately 35-36 hours later. Shortly before ovulation (34-36 hours after the HCG injection), a transvaginal ultrasound examination is performed for retrieval of the eggs (called oocytes). A specially designed needle is inserted into the vagina along the ultrasound probe under local anesthesia to remove the eggs from the ovaries. The follicles are gently aspirated through the needle and the eggs are collected.

After the eggs are aspirated into test tubes, a laboratory specialist (embryologist) carefully examines the eggs for their maturity. The husband's sperm, which are collected about the same time as the IVF egg retrieval procedure, are then separated from the semen in a process called “sperm washing” and mixed in special Petri dishes (or “test-tubes”) with the eggs. The entire IVF egg retrieval procedure normally takes 30-45 minutes and most women leave the clinic within 3 hours of the procedure. The fertilized eggs (called embryos) are carefully grown in the special IVF laboratory for the next 3-6 days.

The woman then returns to the clinic where 1-2 of the embryos are transferred through the cervix up into the uterus in a simple procedure. She then returns home to rest for 1-2 days and then can resume normal activities. Progesterone injections are given for several weeks to increase the chances of successful pregnancy occurring.

What conditions are appropriate for treatment with IVF? IVF is considered appropriate for the following infertility conditions:

1. Mechanical infertility due to tubal obstruction.
2. Oligospermia (low sperm count) or other male infertility problems (with ICSI).
3. Endometriosis (especially after failure of treatment with either drugs or surgery).
4. Ovulation problems such as luteal phase defects after failure of other treatments.
5. Failure of repeated attempts at artificial insemination.
6. Long-term unexplained infertility.

IVF can usually be performed even in the presence of extensive adhesions or scar tissue around the fallopian tubes and ovaries. A woman must have at least one normal ovary and a normal uterus to have a reasonable chance of success with the IVF procedure.

Are there any risks or side effects of IVF? As with any infertility or medical treatment, there are potential side effects and risks of IVF. Ovulation induction with fertility drugs can cause *ovarian hyperstimulation syndrome*. This condition is potentially serious and is due to multiple large ovarian cysts which cause fluid retention and other symptoms. It appears to occur in less than one out of 1000 cycles of women on fertility drugs. In addition, ovulation induction is associated with a risk of *multiple pregnancy*. Of IVF pregnancies, 30% are currently multiple pregnancies. Most of these are twins, but triplets or greater can rarely occur with IVF and may require consideration of multifetal pregnancy reduction to twins.

Ectopic (tubal pregnancy) occurs in about 3-4% of IVF pregnancies. The normal incidence of ectopic pregnancy is about 1-2%. This is a potentially serious disorder which may require surgery. All pregnancies in an IVF program are followed carefully in the first few weeks to watch for ectopic pregnancies. *Miscarriages* appear to occur in about 15-20% of IVF pregnancies. This rate is very close to the normal incidence in spontaneous pregnancies in an IVF patient population (i.e. adjusted for age).

Transvaginal ultrasound egg retrieval is considered a safe minor procedure in which the risk of complications is quite low (less than 1%). Rare complications could include bleeding, infection, damage to the intestines or other organs, and reaction to medications. Side effects may include some slight to moderate abdominal or shoulder pain for a few days.

Why is IVF so expensive? IVF is expensive because of the highly specialized equipment required for an IVF laboratory and because of the large number of highly skilled people needed for this type of program. In addition, almost half of the cost may come from the fertility medications used in an IVF cycle. Although IVF is not a new procedure, it is rarely covered by health insurance and there is no research funding or other outside support. The program must be supported entirely by fees paid by the participants.

What if pregnancy occurs? If pregnancy does occur, you will be followed closely with blood tests and ultrasound examinations during the first 7-9 weeks. This is done in order to diagnose ectopic (tubal) pregnancy, multiple gestation, or other problems as early as possible. After pregnancy becomes established, IVF pregnancy is not different from any other pregnancy for a woman of the same age and health. Once an IVF pregnancy reaches 10-12 weeks of gestation, it should be managed as any other routine pregnancy.