

Getting Pregnant

Notice events of the menstrual cycle are coordinated such that ovulation is expected to occur at about day 14 of a 28-day cycle. An oocyte that has been ovulated survives and remains viable in the fallopian tube for only about 24 hours. If intercourse has taken place, the egg and sperm meet in the outer end of the fallopian tube, where conception may occur. The fertilized egg travels through the tube towards the uterus with the help of tiny hair-like projections called cilia which help move the egg along towards the uterus. The maximum length of time that sperm can remain viable in the female tract is 3 to 5 days. Sperm can reach an egg in the fallopian tube within an hour after intercourse. So, the best time to get pregnant would be if intercourse occurred within a few days before ovulation to a day after ovulation. However, given the variability in menstrual cycles, the optimal time of intercourse to achieve pregnancy has potential for great variability each month.

Once the ovum is fertilized it will complete the 2nd meiotic division and then begin to develop. The journey to the uterus takes about 3 days. As the developing embryo, now called a blastocyst, enters the uterus it floats around for another 3-4 days as the uterus prepares for implantation. The window for successful implantation is relatively narrow and if the blastocyst does not implant at the proper time it will not survive. Typically, implantation occurs 6-7 days after fertilization. Recall that it is at about this time that the corpus luteum begins to regress and estrogen and progesterone levels begin to fall. If they get too low the endometrium will die and be sloughed off, along with the blastocyst. At about the time of implantation cells of the blastocyst begin producing hCG which rescues the corpus luteum so that it continues to produce estrogen and progesterone. Progesterone is particularly important in maintaining the endometrium. As the placenta develops it begins to produce hormones, including progesterone and estrogen, and by the end of the first trimester the corpus luteum is no longer required to maintain the pregnancy. Note, home pregnancy tests check for the presence of hCG. Since it is produced by cells of the embryo it will not be present unless an egg has been fertilized.

References Fehring R., Schneider M., Raviele K. (May 2006). "Variability in the Phases of the Menstrual Cycle ". Journal of Obstetric, Gynecologic, and Neonatal Nursing 35(3). DOI: 10.1111/j.1552-6909.2006.00051.x, <http://dx.doi.org/10.1111/>

Additional Information if interested:

Female Infertility

You have just learned about the many factors and hormone levels that have to come together in just the right time and just the right way for both the mother and the father in order for pregnancy to happen. It is not uncommon for married couples to live together as husband and wife and do nothing to prevent children from coming to their home and still not becoming pregnant after months or years of trying. Because of the risks of hormonal therapy to aid with infertility or with birth control, a married couple may choose first to use their knowledge of the female ovulation and the menstrual cycle to either assist them with becoming pregnant or to attempt to time the coming of their children. If that is not working, then there are hormonal therapies and medical treatments available for both women and men to assist families in becoming pregnant.

Typically, a young couple should seek medical assistance if they have actively tried to conceive for a year without results. Older couples (over age of 30) are recommended to visit a professional after 6 months of actively attempting to achieve a pregnancy. The rationale for this timeframe lies with the age and declination of egg quality in women and the time it may take to achieve success, even with using advanced reproductive techniques. These are guidelines only and every situation is unique and the couple should carefully consider options as they plan to expand their family.

There are many reasons a woman may experience fertility difficulties. Endometriosis, hormone imbalances and ovulation issues can contribute to female infertility. As couples desiring to have children meet with infertility specialists, some of the options used to treat infertility include improving overall health by managing weight, sleep, stress coping, balancing thyroid and reproductive hormones in conjunction with advanced reproductive techniques. Often lifestyle changes can contribute to successful outcomes in artificial insemination (AI) and In Vitro Fertilization (IVF).

Advanced Reproductive Technology (ART)

Using medical assistance to achieve pregnancy is referred to by reproductive care facilities as Advanced Reproductive Technology (ART). The two main treatments for couples with fertility difficulties include artificial insemination (AI) and In Vitro Fertilization (IVF). Depending on the type of fertility, age, health and circumstance of the couple, the medical care provider may suggest one of the other.

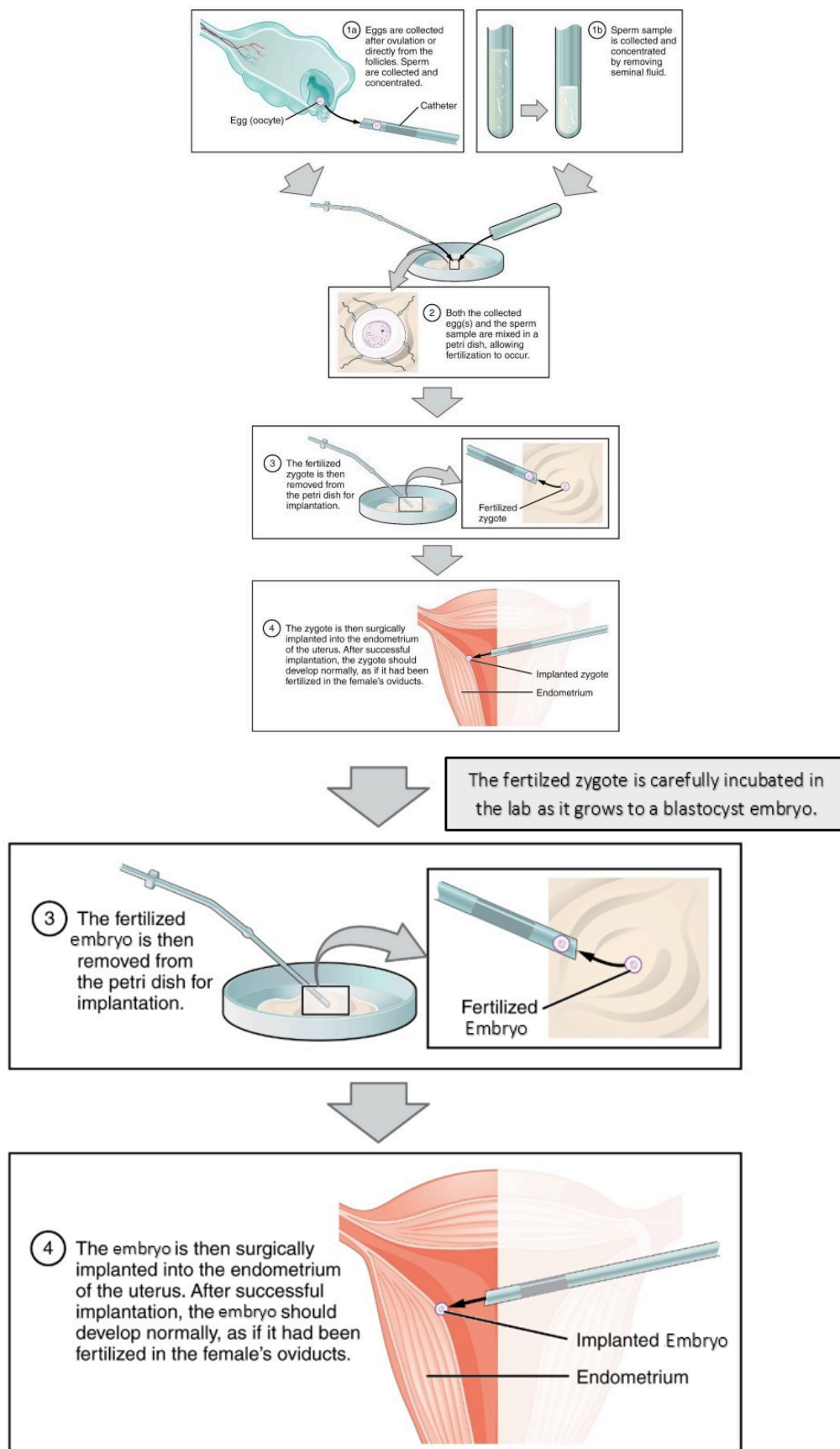
With AI, a man gives a semen sample which is processed in a lab and then is inserted into the woman's uterus using a special catheter. The semen is replaced with special media containing nutrients and buffers for the sperm and they are concentrated into a much smaller volume. It is essential to process the sperm and remove the liquid portion of the semen prior to placement in the uterus to allow more sperm to reach the fallopian tubes. After the procedure the woman can go about her daily activities.

The success rate for AI is approximately 10-20% per cycle for normal sperm samples and with regulated ovulation and may require several attempts before pregnancy results. Artificial insemination can cost about \$400 per attempt as a base price, increasing if monitoring and medication for the female if needed.

In Vitro Fertilization is a more intense and evasive process. A woman is given hormone therapy to first down-regulate her menstrual cycle and then to stimulate the development of several eggs at once. When her estradiol levels and number of follicles approach maturity, she is given a shot of hCG which will mimic the function and role of LH triggering ovulation and the development of the corpus luteum. The first part of the IVF procedure is scheduled and the eggs are retrieved prior to natural ovulation. This is done by using an ultrasound-guided needle, and usually under a light anesthesia. The follicles are aspirated into a tube with the hope that the follicle fluid contains a mature ovum. Each follicle is kept separately and the eggs are located, numbered and transferred to a dish. The husband leaves a semen sample, similar to the process with AI. The eggs are then fertilized with the husband's sperm, either added directly into a dish with several thousand sperm, or by using a process called intracytoplasmic sperm injection (ICSI), where a single sperm is injected into a mature egg. ICSI is very helpful if a man's sperm penetration assay shows his sperm have difficulty penetrating the egg.

The new zygote grows in the lab in a special incubator for 5-6 days until it has developed into a blastocyst embryo. During this time, the female is encouraged to rest and allow her ovaries to recuperate. She will be given progesterone shots to help her body thicken the endometrial lining. Then the second part of the IVF procedure takes place as one, or sometimes two, of the best quality embryos are transferred back into the uterus. Two weeks after the transfer, a blood test will confirm pregnancy. If pregnant, she will continue to take progesterone until an ultrasound at 5 weeks confirms a heartbeat.

IVF costs can vary depending on testing or medications needed, but typically start at about \$12,000 per attempt. The success rate also varies, but established and reputable clinics have a 50% -75% pregnancy rate for women under the age of 35.



Process of In Vitro Fertilization.

Synthetic Hormones

Hormone therapy is the use of synthetic forms of estrogen and progesterone to treat a variety of situations including: infertility due to hormonal imbalance; painful menstrual cycles related to cysts on ovaries or endometriosis; relief of menopausal symptoms; and, most commonly, in the form of hormonal birth control. After studying the relationship of the different hormones involved in the ovarian and menstrual cycle, you can see how a doctor could use these hormones to manipulate ovulation.

Most hormonal birth control works by providing a constant level of estrogen and progesterone which sends a negative feedback to the hypothalamus and pituitary gland preventing the release of FSH and LH and therefore preventing follicle development and ovulation.

Hormonal therapy can also be used to assist a woman with becoming pregnant. A few of the common hormonal infertility treatments include the following:

Clomiphene citrate (Clomid): Inhibits estradiol and acts as an estrogen receptor antagonist in the hypothalamus. This signals the pituitary to release more FSH and LH to stimulate the development of the follicle and trigger ovulation.

Gonadotropins with GnRH agonists: GnRH agonists initially stimulate the release of FSH and LH, but then the overproduction of these hormones lead to downregulation of the receptors and suppression of the production of further FSH and LH. The gonadotropins act directly on the ovaries to stimulate the development of multiple eggs. This medication is given by a series of injections and is typically given during the process of IVF. This medication increases a woman's chance for becoming pregnant with twins or triplets.

Progesterone: Progesterone thickens the lining of the uterus and may be used to help regulate menstrual cycles for those who have stopped menstruating. If a woman is doing IVF, progesterone may be used to prepare the uterus for implantation.

Bromocriptine (Parlodel): Lowers the level of prolactin in the blood. Prolactin levels if elevated can cause irregular menstrual cycles or inadequate luteal phase, which is why many women who are breastfeeding may not experience ovulation or regular menses as their bodies naturally release Prolactin. Bromocriptine is a dopamine-receptor stimulant that acts on the pituitary gland to reduce the production of prolactin.

Corticosteroids: For some women, their adrenal gland may produce excess amounts of androgens, including testosterone and DHEA. In women, testosterone is produced in the adrenal glands and in the ovaries, where it is converted to estradiol, and plays an important role in bone strength, development of lean muscle mass, emotional well-being and energy level. If testosterone levels are too high from excessive amounts of androgens from the adrenal gland it can interfere with the normal follicular development and ovulation. In this situation, low doses of corticosteroids, such as dexamethasone, may be given to lower the androgen levels to a normal range.

There are serious risks related to hormonal therapy that you should be aware of. With any hormonal therapy, both women and men should carefully consider if the benefits outweigh the risks.

Hormonal therapy, including birth control pills, taken over an extended period of time, increases a woman's risk for blood clots, heart disease, stroke and breast cancer. Other side effects include high blood pressure, migraines, benign liver tumors, yeast infections, irregular bleeding, weight gain or water retention, nausea, emotional sensitivity, mood swings and depression.

Role of Birth Control in Fertility

For those in their child-bearing years, the taking of birth control pills may contribute to fertility problems later. After stopping taking oral forms of birth control, the body should typically return to the normal follicle development and

ovulation cycle within a few months. But if a woman uses Depo-Provera, which is a shot of a synthetic hormone similar to progesterone typically given every 3 months to prevent pregnancy, it can take up to 1 to 2 years for the body to return to the normal ovulation cycle in order to get pregnant, and therefore is not a recommended form of hormonal birth control for a woman hoping to get pregnant in the near future.

Male Infertility

Currently, 15 – 20% of married couples, a minimum of 5 to 6 million couples within the U.S. will experience some degree of infertility with all of its accompanying emotions and frustrations. Infertility may be defined as the inability of a couple to achieve conception after one year of unprotected intercourse, or inability to carry direct pregnancy or a live birth. Recent data suggest that young, fertile couples achieve a pregnancy in only 20-25% of properly timed cycles of intercourse. This is due to the fact that any problem with the sperm, egg, embryo development, implantation or maintenance of pregnancy will prevent a successful pregnancy. Any alteration in this complicated sequence of events can disrupt conception or pregnancy and results in infertility. Approximately one third of fertility difficulties are due to female factors, another one third to male factors, and the remaining one third to a combination of male and female infertility and unexplained infertility. Within the past few years, important developments have been made in diagnosing and treating fertility difficulties. Infertility is an area of medical care that is changing and advancing at a very rapid pace.

The semen analysis is the primary test used in the evaluation of male infertility. It is usually the first evaluation for the male investigating infertility with his spouse and can reveal information about the ability of the sperm to reach the site of fertilization. The major parameters of the semen analysis include the sperm concentration, progressively motile sperm count and sperm morphology. Although often emphasized, sperm concentration is not a good predictor of fertility unless it is very low. Other factors that better predict potential fertility include how well the sperm moves in a progressive (forward) direction, the head and tail shape (morphology) and membrane function. Decreases in the sperm concentration and sperm motility affect the motile sperm counts, which reflects the ability of sufficient numbers of sperm to reach the site of the egg and complete the fertilization process. The sperm morphology is very important, and may be indicative of the ability of sperm to fertilize the egg.

It must be emphasized that semen analysis information is limited and that other tests are necessary (such as acrosome reaction, sperm chromatin integrity test, sperm penetration assay) to further determine the ability of the sperm to penetrate the egg once it reaches the zona pellucida (the thick transparent membrane surrounding the ovum).

Semen that is “normal” or “average” in quality may not be the same as that which is potentially fertile. For example, the normal sperm concentration value is considered 15 million/mL by the WHO (World Health Organization), however, this is on the low end. Most men with only 15 million sperm per mL would likely have some type of fertility difficulties since movement and head/tail shapes also have to be taken into consideration.

There may be many reasons a male has fertility difficulties: a varicocele (like a varicose vein in the testes); too high or too low levels of gonadotropins, prolactin and testosterone; inability to undergo the acrosome reaction and capacitation; lack of longevity for the sperm; anti-sperm antibodies (often due to damage with the blood/testis barrier); and genetic factors.



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