In Vitro Fertilization (IVF)
Patient Information

Conception is a complex process that involves many different factors. If one of these factors is impaired, infertility can occur. One in seven couples experience infertility.

In one third of cases, infertility can be attributed to factors affecting women, another third of cases involve factors affecting men. The remaining third of infertility cases can be attributed to fertility issues in both partners, or to reasons unknown.

In-Vitro Fertilization (IVF) is an assisted conception technique available to help people with fertility problems to have a baby. It involves giving the woman fertility drugs to stimulate egg production, and then retrieving the eggs from the ovaries. She is then given hormones to prepare her uterus for pregnancy, while the eggs are fertilized with the sperm in a laboratory. The embryos are then implanted into the woman's uterus, and if all goes well, a normal pregnancy is achieved.

The overall success rate of IVF is ranging between 30% and 40 % per embryo transfer and depends on many factors such as the age of the woman, the embryo quality and the number of embryos transferred.

One of the main factors influencing the outcome of IVF treatment is the age of the woman whose eggs are used, as the quality of the eggs declines as the woman gets older. The rate of birth defects, chromosome abnormality or miscarriage also rises with maternal age.

Couples considering IVF must undergo an assessment at the fertility clinic before any treatment begins. A full lifestyle check-up can help people with fertility problems to optimize their health before treatment starts.

Ovulation Induction

Ovarian stimulation is aimed to mature multiple follicles, each one containing an egg. Before ovulation induction, Diphereline is started, by subcutaneous injection. This medication turn off the normal menstrual cycles and prevent premature ovulation. It may cause mild side effects -- hot flushes, mild headaches, and vaginal spotting.

A vaginal ultrasound and blood tests will be scheduled after 10 to 14 days. Most women are ready to start stimulation immediately, but if the hormone levels are elevated or a cyst is present on the ovaries, another 5 to 10 days of Diphereline treatment may be needed or a cyst aspiration may be performed before proceedings.

Occasionally, if obtaining a sperm sample on the day of egg retrieval might be difficult, the male will be asked to give a backup sperm sample early in the cycle. This will be frozen and stored, to be available as an emergency backup.

Ovarian stimulation protocol is started after the menstrual period with daily injections of gonadotropins (Menopur, Puregon, Gonal-f). Women who are sensitive to the medication need only a small amount of gonadotropins, while those who are resistant require more.
The main risk of gonadotropins is ovarian hyperstimulation syndrome, when too many follicles develop in the ovary. The ovary then grows to a large size and leaks fluids, resulting in nausea and bloating, dehydration, fluid collection around the abdominal organs or ascites. In very severe cases, blood clots and strokes can occur. In rare cases, hospitalization and removal of abdominal fluid may be required to regulate fluid balance. Hyperstimulation may be predicted and controlled by monitoring the ovaries with ultrasound and blood estrogen levels. If the risk is very high, the cycle may be canceled.

When ultrasound examination and estrogen levels suggest that the follicles are large enough and the eggs are mature, one dose of human chorionic gonadotropin (hCG) is given to prepare the eggs for ovulation and fertilization. The timing of hCG is critical, so it must be taken exactly as instructed.

**Oocyte Retrieval**

The egg retrieval is performed thirty-six hours after hCG injection under sedation or general anesthesia. After sedation, the vagina is washed with a salt water solution. A needle is placed under ultrasound guidance into the ovary and fluid and eggs from the follicles in the ovaries are collected into a test tube and sent to the IVF lab. The whole procedure takes about 30 minutes, and discomfort is generally minimal.

Complications after egg retrieval are rare. Unusual problems include internal bleeding, vaginal bleeding, or infection. Recovery after the egg retrieval is quite rapid. Some pelvic heaviness, soreness, or cramping are common. Spotting is normal, but should be less than a normal menstrual period. Most women are able to go home within two hours of the procedure. Someone might be available to take the patient home, since she cannot drive a car after sedation or anesthesia.

The male will collect a sperm sample by masturbation the day of the egg retrieval. He should abstain from ejaculation for 2 to 4 days before giving the sample. Occasionally a second sample on the day of the egg retrieval is required.

**Insemination & Fertilization**

Some of the most important events in your cycle now occur behind the scenes, in the laboratory. Insemination of the eggs with sperm is followed several hours later by fertilization, when the sperm enters the egg.

The stages that follow are very important to the future embryo. After fertilization, the egg looks like a cell with two nuclei, called pro-nuclei (2PN stage). The pro-nuclei join or fuse within a few hours, producing a fertilized egg, or embryo. The embryo can begin cleaving, or dividing, first into two cells, then into four. Embryo transfer typically occurs at 72 hours, three days after egg retrieval. Transfer can also occur at 5-6 days after egg retrieval, when the embryo develops to the blastocyst stage.
Growing the embryos to the blastocyst stage may give valuable information about the potential of the embryos and allows a better selection of embryos available for transfer. Approximately one in ten patients may not make blastocysts by the fifth day.

Problems can occur with fertilization and cleavage. Occasionally sperm are unable to penetrate the egg in the first 24 hours, and a fertilization failure occurs. Most eggs can fertilize only the first day, and a re-insemination or an intracytoplasmic sperm injection (ICSI) the second day doesn't produce more embryos. Sometimes embryos do not divide or stop dividing at an early stage, and a cleavage arrest occurs. Fragmentation or breakage of some of the cells in the embryo is also quite common; severe fragmentation will reduce pregnancy rates, but milder fragmentation is not a serious problem.

Micromanipulation techniques may be used in some case. ICSI (intracytoplasmic sperm injection) is a procedure developed to help couples with male factor infertility or previous low or failed fertilization cycles. With ICSI, one sperm is physically injected into the center of the egg, in order to increase the chances of fertilization. Assisted hatching, in which a portion of the covering of the egg is removed might be performed in order to help the embryo stick to the uterus.

**Embryo Transfer**

Three or five days following the Egg Retrieval, the patient will have the Embryo Transfer (ET). During this time, the embryos have been allowed to grow and divide in the incubator.

Before the transfer, the physician will meet with the couple and discuss the number and quality of the embryos available for transfer. A decision will be made as to the number of embryos that will be transferred and the number to be frozen or discarded. Embryo transfer is a painless procedure. A speculum is inserted in the vagina and the cervix is washed and cleansed. The physician will introduce a catheter through the cervical canal into the uterine cavity where the embryos are released. Ultrasound may be used to guide the transfer catheter.

In an effort to increase the success rate for each couple, multiple embryos are usually transferred; not all embryos that look healthy are capable of making babies. Multiple pregnancy is a risk when several embryos are transferred. However, when IVF is performed, the number of embryos that are transferred can be controlled.

After completing the transfer there is very little to be done to affect the chances of successful implantation. Whether or not the embryo or embryos implant in the uterus is primarily dependent on the health of the embryo.

At home, patient may resume normal activity, but avoid vigorous aerobics, heavy lifting, running, hot tub baths, jacuzzis and swimming. Patients are also advised to refrain from intercourse for one week after the transfer.

Until the pregnancy test patient should take vaginal progesterone to improve the lining of the uterus and help the embryo implant and grow.

It is very common to have a small amount of bleeding during the following weeks. As the embryo implants into the endometrium it may cause a leak in one of the blood vessels in the
uterus. It is not unusual to have symptoms of pregnancy that come and go during this two-week period or to have a sensation of heaviness or cramping in the pelvis. If there are severe symptoms (significant increase in pain, heavy bleeding, a temperature above 38 C degrees, or shortness of breath) it is better to call the clinic.

Cryopreservation & Frozen Embryo Transfer (FET)

If excess embryos are available, they may be cryopreserved for future use. This will reduce the need for multiple cycles of ovarian stimulation and egg retrieval. Placement of the embryos into the uterus requires a normal uterine lining and close synchronization to the normal process of embryo development. Such synchronization will require monitoring via blood tests and ultrasound examination(s). Embryo transfer can be made in a natural cycle; in some cases, an artificial cycle (controlled by medication) is a better option for preparing the uterine lining for implantation. Only embryos considered by the embryologist to be of potential medical use will be cryopreserved or transferred. The cryopreserved embryos will be used according to the directive of the patient and her partner.

Pregnancy Testing

Two weeks after the egg retrieval procedure, a blood pregnancy test is scheduled.

Rising blood levels of the pregnancy hormone, hCG, indicate that implantation has occurred. A pregnancy at this stage is referred to as a "chemical pregnancy". Confirmation of a "clinical pregnancy", the presence of a gestational sac in the uterine cavity, is made by ultrasound 2 weeks after the first blood test.

If the test is negative, the period will start in 2 to 5 days after stopping progesterone medication. It will be scheduled a follow-up visit with your doctor to review the cycle and make plans for the future.

Even if a pregnancy is successfully established, multiple pregnancies, miscarriage, ectopic pregnancy, still birth, or birth defects may occur. Approximately 25% of these pregnancies may result in miscarriage

Multiple gestations are associated with increased risk of miscarriage, premature labor, cesarean section, blood loss, significant maternal, fetal or newborn health risks.

The risk of birth defects from embryos formed through IVF is similar to natural conceptions. The expected rate of major birth defects in the normal population is 2-4%. Available information is currently too limited to completely discount the possibility of risks to the fetus related to micromanipulation (ICSI) or cryopreservation.

Undergoing IVF or other assisted conception procedures can be emotionally and physically draining, especially when pregnancy was not achieved. However, it is not uncommon for couples who have been successful in their attempts to start a family to find it difficult to adjust to their new life. It is important to seek help from health professionals or contact a fertility support group; talking with others who can empathize with these experiences can also be helpful.