

Global Fertility Services

PLEASE READ THIS MEDICAL INFORMATION

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This handout gives a basic outline of In Vitro Fertilization (IVF) then covers the process in more detail. It relates the process of screening in preparation for a cycle, the cycle of treatment itself, and the oocyte retrieval. It describes the preparation, techniques, and tests for in vitro fertilization and offers suggestions on maintaining low stress levels while going through the cycle. Every cycle is different; use this handout as a guide and please ask questions of the nurses and physicians as they arise.

In vitro fertilization, often referred to as IVF or IVF-ET (embryo transfer), is the high-tech way of producing pregnancies. IVF involves removing eggs from a woman's ovaries and combining them with sperm in the laboratory. The words "in vitro" mean literally "in glass," as in a culture dish. The sperm fertilize the eggs in the dish to form embryos, or fertilized eggs, that are then transferred into the uterus with a catheter or small tube.

Here is an outline of the basic steps in IVF:

Pre-Cycle Preparation: A nurse coordinator schedules the cycle, reviews consent forms, and answers any questions. A set of screening tests are performed to maximize fertility. Oral contraceptives (birth control pills) are started in the month before the treatment cycle. Oral contraceptives help to regulate menstrual cycles, making the date of the menstrual period more predictable and smoothing the ovarian response to fertility drugs. Lupron or Synarel, medications to prevent early ovulation, are started just before finishing the oral contraceptives.

Ovulation induction: Fertility drugs stimulate from one to forty follicles in the ovaries, each containing a single egg. The eggs are ones that would be available only in the current cycle. We cannot mature eggs that might be available for maturation in future cycles.

Oocyte retrieval: Oocyte retrieval is removal of the eggs from the ovaries. A needle is guided by ultrasound into each follicle in the ovary to remove the fluid containing the egg. The ultrasound is performed vaginally - neither incisions nor surgery are required, but sedation is recommended.

Insemination and Fertilization: The eggs are inseminated, meaning that they are mixed with a sperm sample. Insemination is followed by fertilization, when the sperm combines with the egg, resulting in an embryo, or zygote.

Embryo transfer: Embryos are placed into the uterus or womb of the Intended Mother or Surrogate using a catheter, a very small soft plastic tube. The catheter is designed to be small and flexible, and slips easily through the cervix. This is a minor procedure that seldom requires anesthesia or sedation.

IVF Screening

Before you begin the egg donor cycle you will go through a screening process to ensure that everything is optimal for success. This process may take 2-3 weeks. At your initial visit, you will meet with the physician who will take a detailed history and

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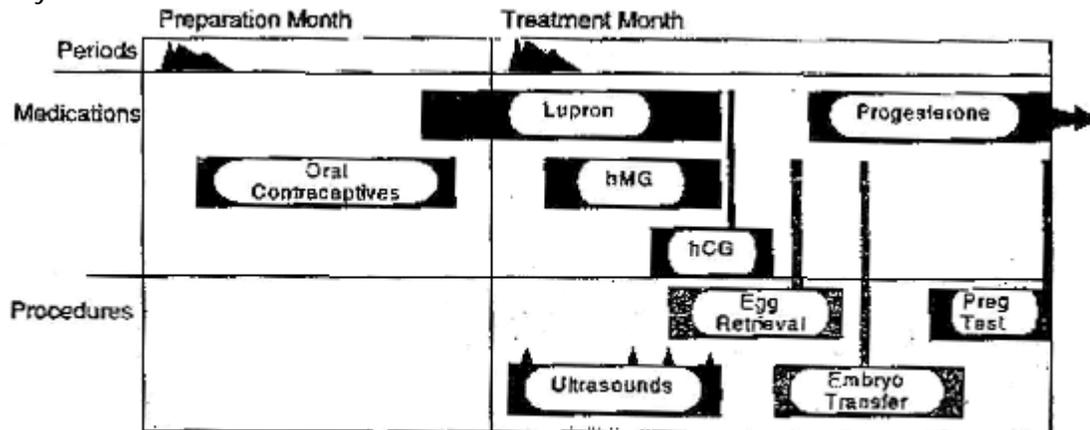
explain the process of in vitro fertilization and embryo transfer. He or she will order various tests and arrange a visit with the nurse coordinator. A blood sample is drawn to test for blood type and certain infectious diseases (such as hepatitis and HIV).

The IVF Cycle

Ovulation Induction

Ovulation induction is the stimulation of the ovary to produce multiple follicles each containing an egg. In the month prior to ovulation induction, oral contraceptives are given as a gentle means of preventing ovarian cysts, which are fluid sacs in the ovary. Such cysts, which were common prior to use of oral contraceptives, delayed the start of the cycle and interfered with normal ovarian function. Cysts are rare when oral contraceptives are used.

A few days before finishing the oral contraceptives, Lupron or Synarel is started. These are medications that prevent premature ovulation. Lupron and Synarel are very similar, but Lupron is taken by subcutaneous injection, and Synarel by nasal spray.



The events of an IVF cycle

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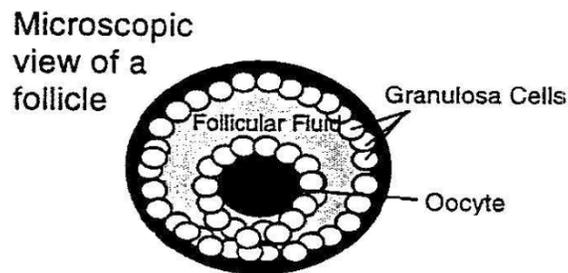
Lupron and Synarel may cause mild side effects - hot flashes, mild headaches, and vaginal spotting a week to 10 days after beginning the medication; these symptoms are normal, and are signs that the medication is working. Please be certain that you are not pregnant prior to starting Lupron, since these drugs can interfere with the normal hormones that support early pregnancy. (Note that Lupron is discontinued before the hCG is given).

The nurse coordinator assigns a date for a vaginal ultrasound and blood test around the time the period starts. Using vaginal ultrasound, the ovaries are examined for ovarian cysts, small fluid pockets that appear occasionally after using Lupron or Synarel. Cysts often disappear on their own, but a cyst may be aspirated (removing the fluid) to help it collapse faster. The blood test measures estrogen, a hormone produced by the ovary. Most women are ready to start stimulation immediately, but if the estrogen level is elevated or a cyst is present on the ovaries, you may need

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another 5 to 14 days of Lupron treatment before proceeding.

Daily or twice daily injections of human menopausal gonadotropins, the fertility drugs, are started just after the menstrual cycle. The most commonly used drugs are the recombinant FSH agents, such as Gonal-F and Follistim. The older medications Metrodin (urinary FSH), and Pergonai, Repronex, and Humegon (urinary menopausal gonadotropins) are occasionally used. These medications are concentrated forms of the natural hormones which stimulate ovulation in a normal menstrual cycle. The newer drugs are more purified, and can be given just under the skin with a tiny needle (subcutaneous injection). The older medications are given into the muscle of the buttock or upper arm (intramuscular injection) with a larger needle. Although these are different medications, there are only small differences in the way the body responds to them, so we will refer to all of them as gonadotropins in this handout. The day gonadotropins begin is stimulation day 1, or "stim day 1" regardless of when it occurs after the period. The Lupron dose may be reduced when stimulation starts.



The follicles are fluid-filled sacs inside the ovary. There are hundreds of thousands of follicles in each ovary, but only a few grow large enough to appear on an ultrasound exam, and only the large follicles hold mature eggs. The eggs are about a tenth of a millimeter in diameter, just under a size that is visible to the naked eye, so the actual egg cannot be seen on ultrasound. The follicle is about two hundred times bigger than the egg, and can be seen clearly when it is large enough. Each follicle usually contains one egg surrounded by granulosa cells. Granulosa cells surround the egg, produce the follicular fluid, and support the egg in its development. In the normal menstrual cycle, only one follicle matures, reaching about an inch in diameter.

Occasionally a follicle may not contain an egg, and even more rarely there may be two or more eggs per follicle. Gonadotropins cause several follicles to enlarge at once. The number can vary from one or two to 30-40 in some women. The dose of gonadotropin is based on a prediction of how the ovaries will respond, and varies from one ampule a day to 10 or more ampules per day. Women who are very 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. Ovarian hyperstimulation occurs 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, and, if severe, fluid collection around the abdominal organs, or ascites. In very severe cases, fluid collects around other organs, such as the lungs and heart, and blood clots and strokes can occur. If the ovary enlarges too much, rupture of the ovary and abdominal bleeding can occur. Fatalities have been reported, and hospitalization is

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sometimes required to regulate fluid balance.

Fortunately, serious cases of ovarian hyperstimulation are quite rare, and your doctor can predict and prevent hyperstimulation by monitoring the ovaries with ultrasound and blood estrogen levels. Removal of the granulosa cells during egg retrieval reduces the risk of hyperstimulation, so the risk with in vitro fertilization is lower than with gonadotropin use for simple ovulation induction. If the risk is very high, a cycle may be canceled. Although this is a rare event, it provides complete safety, in that hyperstimulation does not occur after a canceled cycle.

When ultrasound examination and estrogen levels suggest that the follicles are large enough and the eggs are mature, you will stop Lupron and gonadotropins and take on a dose of human chorionic gonadotropin (hCG). HCG prepares the eggs for ovulation and fertilization. Ovulation normally begins about 40 hours after the hCG injection, so egg retrieval is performed at about 36 hours after hCG. The timing of hCG is critical, so you need to take it at the exact time you are given.

Oocyte retrieval:

From midnight before the egg retrieval you should not have anything to eat or drink, including coffee or water. If you are taking medications for any other reason, talk with your doctor or nurse about taking the medication on the day of the egg retrieval.

During the egg retrieval you may be given antibiotics or other medications, so make sure your doctor knows about any allergies or medical problems you have.

Thirty-six hours after hCG injection the egg retrieval is performed under sedation or, occasionally, epidural anesthesia. Sedation is medication given through an intravenous catheter, a small tube in an arm vein. You will be asleep and will remember very little of the retrieval. You will not receive general anesthesia so you will be breathing independently. Epidural anesthesia is produced by injection of an anesthetic into your back, numbing the nerves to your ovaries and pelvic organs.

After you are sedated, the vagina will be washed with a salt water solution. A needle is then placed under ultrasound guidance into the ovary. The fluid and eggs from the follicles in your 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.

The egg retrieval rarely can result in complications, such as pain in the ovaries, infection in the pelvis and ovaries, and injury to the bowel, bladder, ureters, ovaries, or major blood vessels. Since your doctor can see the needle on the ultrasound and uses the ultrasound to guide the procedure, the chance of a serious problem is small. Unusual problems include injury to the egg or its covering, the zona pellucida, when removed. On average, two-thirds of the follicles produce eggs, but rarely no eggs are recovered despite complete removal of the fluid in the follicle. Occasionally patients have empty follicles, without an egg, and sometimes the egg is held so tightly to the follicle wall that it is not released when aspirated.

Recovery after the egg retrieval is quite rapid. Some pelvic heaviness, soreness, cramping, or spotting are common. Spotting is normal, but should be less than a normal menstrual period. Usually the discomfort responds to a heating pad and rest, but pain medication is available. Most women are able to go home within two hours of the procedure. Make sure someone is available to take you home, since you cannot

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drive a car after sedation or anesthesia.

Don't plan on doing any work on the day of the egg retrieval. Avoid heavy lifting and vigorous exertion. Walking is fine, just don't overdo it. Avoid tub baths, hot tubs, Jacuzzis, swimming, or immersing yourself in water from the time of the egg retrieval for one week. Take showers rather than baths. Avoid medication except that which your reproductive endocrinologist or nurse has asked you to take. Sexual activity is okay as comfort permits. We do suggest using condoms even during the first month afterwards if you are returning to the use of birth control pills. If you are not returning to

birth control pills please use other methods of birth control (e.g. diaphragm and/or condoms) diligently to avoid unplanned pregnancies. With your first menstrual period after the egg retrieval (usually 10-13 days later), call your doctor at the IVF program to

schedule a follow-up ultrasound.