

DONOR EGG PROGRAM

The decision to use Donor Eggs is a difficult one; the couple may have already undergone many cycles of treatment and many disappointments in their quest for a child. The information contained in this booklet gives an overview of the methods involved in selecting and utilizing an anonymous donor.

The oocyte (egg) donation program at the Fertility & IVF Center of Miami is designed to assist couples with specific reproductive problems due to a woman's inability to produce oocytes to achieve conception. Many of these women have undergone premature ovarian failure (where the ovary stops producing eggs), either due to natural early cessation of ovarian function or due to exogenous causes such as previous chemotherapy or radiation therapy. In addition, some women have ovaries that cannot be adequately stimulated for in vitro fertilization and require the use of a donor, while other women may have a transmissible genetic problem which precludes use of her own oocytes to achieve a pregnancy. The woman who receives the oocyte is called the recipient, while the woman who donates the oocyte is called the *donor*.

The donor egg program is being structured in a similar vein to donor sperm programs which have been in existence in multiple centers throughout the country for many years. The purpose is to provide a healthy number of oocytes to the recipient while optimizing anonymity between donor and recipient. To help achieve this goal, recipients will have no knowledge of the donor's name or address. They will know the donor only by a code number. Similarly, the medical record of the donor and recipient will not reflect the nature of the other. All attempts will be made by the Fertility & IVF Center of Miami team to stagger visits of donor and recipient so that direct contact is not made.

Recipients prepare for treatment by completing all required female and male prescreening tests and attend a consult with a psychologist who is well versed in the issues and concerns that pregnancy through egg donation raises. A consult is also scheduled with our financial department to review expected costs for the treatment.

All recipients meet with one of our egg donor coordinators for a consult. During this consult, discussion takes place regarding the donation process, consents, hormone replacement therapy and protocol, and medications used during the cycle. At this time, the recipient couple discusses the characteristics they are searching for in a donor and the available donors in our pool. Recipients are offered all available profiles of donor that match the recipient's characteristics or requests.

The Fertility & IVF Center of Miami continually recruits donors from the Miami and Broward area. Donors are less than 33 years of age, in normal reproductive health with normal family reproductive and genetic history and no psychological impediments.

Our donors undergo an initial screening process, which involves:

- Extensive review of medical history forms
- Consult and exam with our physicians
- Consult with a psychologist
- Written psychological screening
- Hormonal testing
- Cervical culture for Gonorrhea, Chlamydia, and routine.

Once the donor is selected the rest of the screening is performed and it includes the following tests:

- Chlamydia and Gonorrhea
- HIV I and II antibody screen
- HIV /Hep C screen by PCR
- Complete blood count
- Chemistry panel
- Hepatitis B and C
- Treponema Pallidum (syphilis)
- Sickle cell screen
- Fragile X syndrome
- Cystic fibrosis

Donors are tested a second time for infectious diseases a few days before the retrieval of the eggs. They sign an informed consent to participate in the program. They are offered an honorarium in the amount of \$6,000 for a completed cycle of egg donation. A completed cycle is one in which mature eggs are harvested by transvaginal ultrasound guided oocyte retrieval. We anticipate that approximately 85 percent of cycles will continue to the point of oocyte (egg) retrieval in the initial ovarian stimulation.

Approximately 15 percent of the time, the ovarian response to the fertility medications is not adequate, resulting in a canceled cycle. Normally, the donors are given a portion of the honorarium (\$1,500) to compensate them for their time and commitment up until the point of cancelation.

PREPARATION FOR OOCYTE RETRIEVAL

In the normal menstrual cycle, a woman produces only one oocyte. To increase the chance of pregnancy with donor eggs, multiple eggs are required so that more than one embryo can be transferred into the recipient's uterus. In order to increase the number of oocytes produced, the ovaries of the donor will be stimulated with fertility medications called gonadotropins.

Donors are instructed to begin daily injections of the drug Lupron a week before they expect their period. Lupron is used to down-regulate or suppress the activity of the pituitary that controls the ovaries, so that it does not interfere with the treatment. A baseline ultrasound and blood work is performed with the onset of menses to verify that down-regulation/suppression was achieved. If the estrogen level is low and the ultrasound shows no cysts in the ovaries, then fertility drugs will begin.

The first day of fertility drugs is arbitrarily defined as cycle day 3. On cycle day 7 of the treatment cycle, a second visit for estradiol (E2) blood testing and pelvic ultrasound is performed. At this visit an assessment is made as to the adequacy of follicular stimulation. Totally inadequate stimulation cycles are canceled at this point. More commonly, the stimulation of the donor continues for a total of 10 to 12 days.

Once the physician determines that the follicles in the donor's ovaries have reached the appropriate size and there is an adequate hormone level, the donor is given an injection of hCG. Once hCG is given, ovulation will take place approximately 36 hours later.

In order to capture the eggs prior to ovulation, oocyte harvesting takes place approx. 35 hours after the hCG injection. Oocytes are harvested by transvaginal ultrasound retrieval. The oocytes are retrieved by placing a needle through the back of the vagina directly into the ovary under ultrasound guidance. This procedure is carried out in the Center with an anesthesiologist present to provide intravenous sedative anesthesia. The follicle or sack of fluid in which the egg sits, can be easily seen on ultrasound and aspirated. The embryologist identifies and retrieves the eggs from the aspirated fluid. The recipients are informed of the number of eggs retrieved the morning of the procedure. That same morning, the male partner will provide a sample of sperm. The eggs are later inseminated with the recipient's partner's sperm.

The next morning the recipient couple is informed of the number of egg fertilized.

Complications relating to either follicular stimulation and/or oocyte aspiration are rare but may include:

Unwanted Pregnancy: Inadvertent pregnancy in the donor is best voided by abstaining from intercourse prior to starting medications and until after she begins menses. Using barrier contraceptive throughout the cycle will further minimize this risk.

Ovarian hyperstimulation syndrome: Prior to the use of hormonal testing and ultrasound monitoring of follicular stimulation, this potential complication was more common. With the advent of careful monitoring, severe ovarian hyperstimulation syndrome rarely occurs (1 -2% of cycles).

Complications of oocyte harvesting: Potential complications that have been described in the literature include pelvic infection, which from a theoretical basis could damage the donor's reproductive system, and internal hemorrhage, which would require laparoscopic evaluation and potential surgical correction. To minimize the chance of infection, prophylactic antibiotics are given at the time of oocyte retrieval. This has been quite successful in preventing unwanted pelvic infection.

Risks of ovarian cancer: Controversial data exists that associate ovarian stimulating drugs like gonadotropins to the risk of future ovarian cancer. Until further research is available to clarify the issue, it is the Center's feeling that all fertility drugs need to be used prudently and be appropriately monitored for a limited amount of time.

HORMONE REPLACEMENT FOR EMBRYO TRANSFER

The recipient prepares her uterus for the transfer of the embryos while the donor undergoes stimulation with fertility drugs. The goal is to re-create the hormonal changes that occur normally during a menstrual cycle by administering appropriate doses of estradiol and progesterone. The desired effect on the uterus is the development of an appropriate implantation bed (uterine lining), capable of receiving an embryo. Estrogen is usually administered using patches (Vivelle dot) or in some instances orally. The use of the patch has the advantage of producing more consistent blood levels throughout the cycle and avoids the need for the oral intake of daily medication. Since hormone levels normally vary throughout the cycle, the number of patches will vary in a manner designed to increase the dose of estrogen.

The recipient also begins subcutaneous daily injection of Lupron to suppress ovarian activities a week before expected menses. Once the recipient's period begins, a baseline ultrasound and blood work is performed to ensure that Lupron

has achieved down-regulation. Once down-regulation is confirmed, the recipient begins patches on a determined day designated as Cycle Day 1. It is very important not to begin any patch therapy until the donor is ready to be stimulated. On Cycle Day 13 the recipient attends the office for an ultrasound and an estradiol level to ensure the adequate development of a uterine lining and proper levels of estradiol. If these tests are within normal limits, the recipient remains on the same medication regime or “holding pattern” until the donor is ready for retrieval.

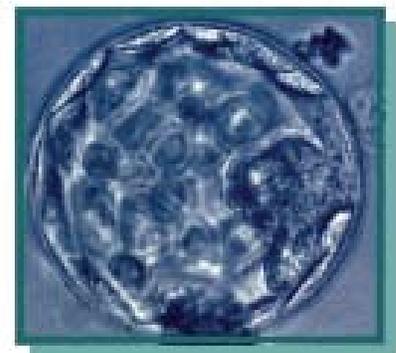
Once the eggs are retrieved, the recipient begins nightly intramuscular injections of Progesterone. Progesterone is a steroid hormone that primes the uterus for embryo implantation.

The fertilized eggs are left in culture to develop for 3 days. On the third day, the embryologist will observe the embryos and note the number, quality, and stage of development. Together with the physician, they will make a recommendation to leave the embryos in culture for an additional 2 days or transfer them that day. If a large number of good quality embryo exists, the embryos can be left in culture for an additional 2 days so that they may reach the stage of blastocyst.

What are Blastocysts?

Blastocysts are embryos that have developed for 5 to 6 days after fertilization. A healthy blastocyst is ready to hatch from its outer shell by the end of the 6th day and implant into the endometrial lining within 24 hours. Currently only about 20-40% of embryos mature into blastocysts, but those that do survive have a better chance to implant and develop into a baby. Why transfer blastocysts? Blastocyst culture can provide a natural selection of the best embryos instead of random selection among good quality embryos on “day 3”. Blastocysts are a viable option whenever a good number and quality of embryos exist. When only a limited number of embryos are available on the third day, there is no advantage to continue culture to a blastocyst.

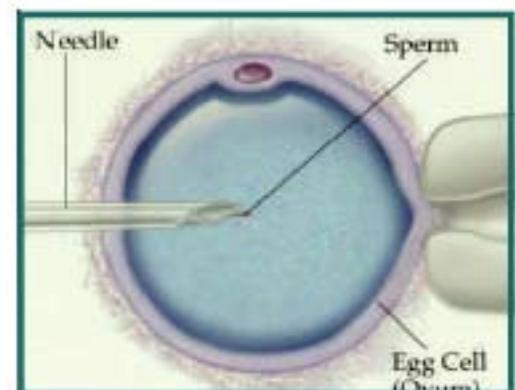
Since blastocysts have a higher potential for implantation, fewer of them are transferred, generally two. Transferring fewer embryos translates into a lower risk for multiple pregnancy, and this is paramount for those couples that want to avoid selective reduction.



Human blastocyst

What is Assisted Fertilization?

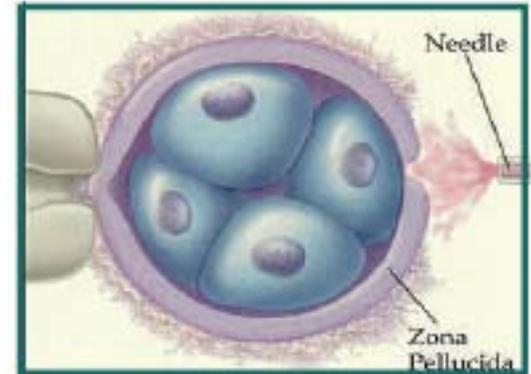
In some cases of male infertility, the usual mixing of egg and sperm may not result in a fertilized egg. A technique termed ICSI (intracytoplasmic sperm injection) in which a single sperm is injected directly inside the egg with a microscopic needle, may offer a solution to those with severe male infertility. This technique is performed in the laboratory the day of the retrieval using mature eggs.



What is Assisted Hatching?

When the embryo is ready to implant, it hatches out of the outer shell and begins to burrow in the uterus. Assisted hatching is a procedure performed by the embryologist under the microscope which involves making a small tear in the protective outer coating of an embryo to facilitate hatching. In older patients and in cases of previously failed IVF attempts, assisted hatching may improve the chances of the embryo implanting into the womb. Assisted hatching is not performed on “fresh” (not previously frozen) blastocysts.

Patients prepare for assisted hatching by taking antibiotics and steroid pills starting a day before the transfer and continuing for a total of 4 days. These measures are taken to protect the embryo from possible immune or bacterial assaults once they are transferred.



EMBRYO TRANSFER

The Center recommends transferring three to six embryos during an assisted reproduction procedure. As a general rule of thumb, pregnancy rates of approximately 7% per embryo can be expected. However, beyond the 3-6 embryo range, the continued increase in the number of embryos being transferred does not increase the pregnancy rate significantly. As the number of embryos transferred increases, the multiple birth also increases. While the presence of twins is often a welcome complication of assisted reproduction, the presence of triplets, quadruplets or more may present considerable obstetric and neonatal problems.

The number of embryos transferred to the uterus must be limited to avoid multiple pregnancy. However, the number of eggs harvested often presents the opportunity to produce more embryos than needed. If the couple chooses, the extra embryos can be cryopreserved or frozen, future egg retrievals.

Transfer of embryos is performed in our office in specially outfitted rooms. An ultrasound is performed to verify the curvature of the cervix. The doctor places a speculum in the vagina and washes the cervix before introducing an empty catheter. This “practice run” will help the doctor place the catheter loaded with the embryos with ease. Following the transfer, the patient rests for 1 hour and then is discharged home. A pregnancy test is performed in the office 2 weeks after the eggs were retrieved.

If pregnancy is established as documented by blood testing following embryo transfer, both estrogen and progesterone will need to be continued through the 10th-12th week of pregnancy. The details of this hormone replacement schedule and the testing required to monitor appropriate replacement will be provided once a pregnancy is established. After the first trimester of pregnancy, the growing placenta produces all the necessary hormones required for sustaining fetal development. It is after this period that hormonal support can be discontinued gradually.

SELECTIVE REDUCTION

Selective Reduction is a technique that is used when multiple embryos have implanted as the result of assisted reproductive technologies. It is a procedure where the extra embryos can be selectively aborted. Selective reduction is usually performed between 9 and 12 weeks gestation. It is done on an outpatient basis by inserting a needle guided by ultrasound either through the abdomen or vagina to inject potassium chloride into the fetus. The incidence of miscarriage associated with this procedure is 4 to 5 percent. Premature labor occurs in about 75 percent of multi fetal pregnancy reduction pregnancies. Miscarriage of the remaining fetuses and maternal infection rarely occurs. The decision of whether or not to undergo selective reduction can be a traumatic one and couples who have invested time and effort to achieve pregnancy may be often unprepared to make this choice. If this procedure is morally or ethically unacceptable, then the number of embryos transferred should be strictly limited. Blastocyst culturing can be an option for those couples that do not wish to do selective reduction. It is helpful for couples considering selective reduction to undergo professional counseling prior to the procedure.

Success rates can vary from couple to couple therefore it is recommended that the Doctor is consulted directly regarding each couples potential for pregnancy.