



DONOR EGG IVF

INDICATIONS

Donor eggs are indicated in any situation where the probability of a successful normal pregnancy using the woman's own eggs is low or non-existent. The standard indication for donor eggs is poor egg quality or lack of eggs (menopause). Since, the uterus generally remains functional despite poor egg quality, substituting donor eggs can restore an opportunity for pregnancy.

ADVANCED REPRODUCTIVE AGE

ARA is probably the most common indication for using donor eggs. Under natural conditions, a woman gradually loses her fertility potential although a number of studies suggest that the loss of fertility accelerates after age 37-38 (see data below). By age 40-44, a woman's fertility is only about 5% of the peak fertility at age 20-24 years. Combined with tests for ovarian reserve, the success rate from using donor eggs usually exceeds the success rate for using a woman's own eggs and certainly for any woman over 38-40. Nevertheless, success rates are not the only determination for undergoing treatment and many women try at least once with their own eggs before opting for donor eggs.

POOR OVARIAN RESERVE

Poor ovarian reserve refers to poor fertility potential. Poor ovarian reserve is closely linked to advancing reproductive age. However, some younger women also demonstrate evidence of poor fertility and a low likelihood for success with their own eggs. We diagnose poor ovarian reserve on the basis of a combination of a history of low egg production in prior IVF cycles, measuring small ovarian volumes or few antral follicles on ultrasound, elevated levels of estrogen in the early follicular phase, and elevated FSH levels in the early follicular phase or in response to clomiphene stimulation (CCT).

PREMATURE OVARIAN FAILURE

Premature Ovarian Failure (POF) refers to early menopause which could be considered the most severe form of poor ovarian reserve. The normal age for menopause is 51 but traditionally we diagnose POF when menopause arrives before age 40. We generally reserve this term for women who have the hallmarks of menopause; lack of menstruation and elevated FSH levels with or without other symptoms such as hot flashes.

GENETIC DISORDERS

Occasionally, a woman will have genetic disorder that either results in POF, recurrent miscarriages or a high probability of genetic disease in any children. In such situations, using a donor egg alleviates the risk of an affected child and corrects the POF induced by the genetic abnormality.

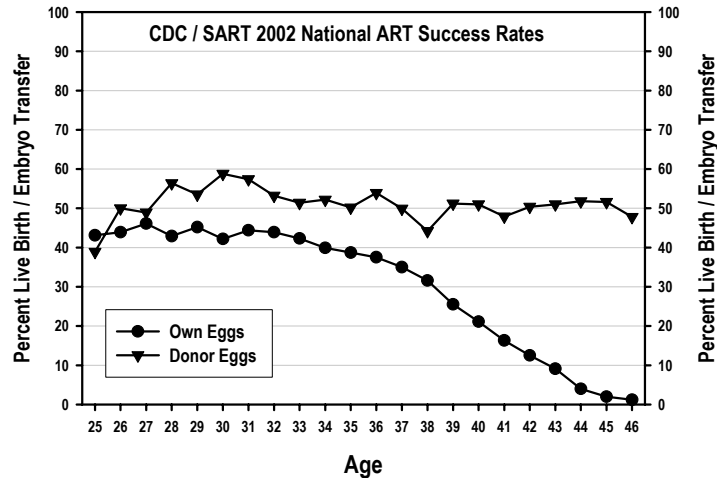
The X chromosome carries genes necessary for egg production. Women who have a single X chromosome (Turners syndrome) or an abnormal X chromosome have POF at varying ages. Donor egg IVF provides these women with an opportunity to become pregnant. Turners syndrome patients may have complicated pregnancies and should seek counseling with a maternal fetal medicine specialist before treatment.

Women with a balanced translocation produce a very high proportion of abnormal eggs and embryos. Some of the translocations lend themselves to PGD (see PGD section for details) and we can identify the few normal embryos for transfer thus avoiding additional miscarriages. However, some translocations cannot be treated with PGD because the genetics team cannot obtain genetic probes. Some women produce only abnormal embryos and we cannot use PGD to obtain a normal pregnancy. Donor eggs are useful in these cases as well.

Another rare genetic disorder includes those women who carry mutations in the DNA located in the mitochondria (the part of the cell that produces energy). A person receives all their mitochondria from their mother, thus if the mother carries a genetic defect in the mitochondria, the child could have a metabolic disease. The genetics of these disorders are complex and varied, so careful genetic counseling is necessary before making any decision. PGD may also be possible for this disorder in the near future. Donor egg IVF provides one treatment alternative.

SUCCESS RATES WITH IVF USING DONOR EGGS COMPARED TO CONVENTIONAL IVF WITH OWN EGGS

The following chart compares the success (measured as a delivered pregnancy) using donor eggs compared to using a woman's own eggs.



From this table, one can see that using the eggs of young, healthy non-infertile women imparts a higher probability of success at almost all ages where a comparison is possible.

At older ages, the discrepancy is even greater than portrayed in this graph because some women do not get an embryo transfer. The incidence of cycle cancellation and the number of cycles with no embryos for transfer rises with the woman's ages when using the woman's own eggs.

Age	No Egg Retrieval	No Embryo transfer
<35	9%	5%
35-37	13%	4%
38-40	17%	5%
41-42	20%	7%
>42	24%	11%

Data from 2002 CDC SART National Success rates

These data suggest that donor eggs result in very high rates of delivered pregnancies. Further, because the eggs come from young women, the incidence of miscarriage and births of chromosomally abnormal children like Down's syndrome is lower. These pregnancies do not require prenatal genetic testing with either amniocentesis or chorionic villus sampling.

WHAT IS THE PROCESS FOR USING DONOR EGGS?

- A donor egg cycle is slightly different than a conventional IVF cycle. Each step will be described in more detail after this outline.
- The patients and physician decide that donor eggs are the best treatment option.
- The patients (donor egg **recipients**) begin **selecting** potential egg donors.
- The NCRS staff and potentially an egg donor agency work with the patient to **match** with an egg donor.
- The patient and donor's menstrual cycles are **synchronized**.
- The donor begins IVF stimulation and monitoring leading to egg retrieval.
- The recipient begins hormone replacement for **controlled endometrial development (CED)**.
- We retrieve the donor eggs and combine them with sperm from the recipient's partner or donor sperm to allow embryo formation.
- The embryo transfer issues are similar to conventional IVF except that with a much higher success rate (implantation rate per embryo), we must be careful to limit the number of embryos transferred.
- The recipient does not make any of her own hormones in a CED cycle, consequently, she must continue the hormone replacement rigorously until 10 weeks of pregnancy, by which time the pregnancy produces its own hormones.



SELECTING A DONOR

Ideal egg donors are young healthy women without a history of infertility or other reproductive disorders. Egg donors do not necessarily need to have had their own children. An ideal egg donor should also have family history free of significant genetic diseases including no close relatives with breast cancer, alcohol or drug dependency, or serious learning or developmental problems. Egg donors should be screened for general health issues, sexually transmitted diseases and carrier status of several common genetic defects and have a karyotype for a chromosome analysis.

Egg donors fall into one of two basic categories: known or anonymous. Known donors usually are family members or close acquaintances. However, some patients recruit their own donors and meet them which also qualifies as a known donor situation. Most egg donors are anonymous meaning that the recipients will never meet the egg donors although increasingly, the recipients do see adult pictures of the donors before making their selections.

The amount of information available to the recipients varies by egg donor agency. Individual recipients must determine for themselves whether they are comfortable with the amount of information that they receive. Some recipients contract with egg donor recruiters who specialize in identifying women with specific criteria to act as an egg donor.

Presented with a list of potential egg donors, the recipients then usually select several potential donors to see which ones are available.

MATCHING PROCESS

The matching process closely related to the selection process. The staff of the donor agency helps to answer questions regarding the potential donors so that the recipients can rank order their initial list. Further, the matching process involves determining when the donors are available for a cycle. Some donors may be in school and want to wait for specific times of the year. Other may be in cycle with another recipient and a waiting period is necessary before she can cycle again (assuming that she is willing – another factor to be determined by the staff).

A match occurs when the recipients agree to use a specific donor and the donor agrees to a cycle.

SYNCHRONIZATION OF CYCLES

The medical portion of the cycle requires “synchronizing” the menstrual cycle of the donor and the recipient. We use medications such as oral contraceptive pills (OCP) and GnRH agonists like Lupron to “down regulate” or shut off the natural reproductive hormones. When both women are down regulated or suppressed then each woman can start her portion of the IVF cycle. The length of time to down regulate varies from 2-4 weeks. In some cases, the recipient is already menopausal and on hormone replacement therapy. Synchronization is much quicker in these situations.

DONOR IVF CYCLE

The egg donor undergoes a very conventional IVF stimulation and egg retrieval process. Please refer to the IVF Fact Sheet for more details. The donor stimulation involves injectable hormones to recruit as many mature eggs as possible. We average about 20-24 eggs per retrieval, of which some might be atretic (dead) or immature leaving about 16-20 healthy mature eggs.

The stimulation process takes about 10-14 days to get to egg retrieval. Once we retrieve the eggs, the donor’s contribution to the cycle is over.

Donors are compensated several thousand dollars for each cycle. The fee paid to the donor compensates her for the injections, multiple visits for blood samples and vaginal ultrasound examinations and undergoing conscious sedation and egg retrieval.

RECIPIENT CONTROLLED ENDOMETRIAL DEVELOPMENT (CED)

The recipient must have an endometrium that is receptive to the embryo to facilitate implantation. Remarkably, we can prepare the endometrium of almost all women to receive an embryo and allow implantation and normal pregnancy. We use estrogen for the initial development which mimics the natural menstrual cycle. We administer the estrogen by mouth most times but may also use transdermal or injectable estrogen in certain situations.

We monitor the recipient’s response to the estrogen by measuring hormone levels and more importantly, the thickness of the endometrium by ultrasound. To increase our success with the donor egg CED cycle, we usually perform a “mock cycle” in which we perform CED to ensure a proper response before the real cycle when we would not have the opportunity to correct a poor response before egg retrieval.

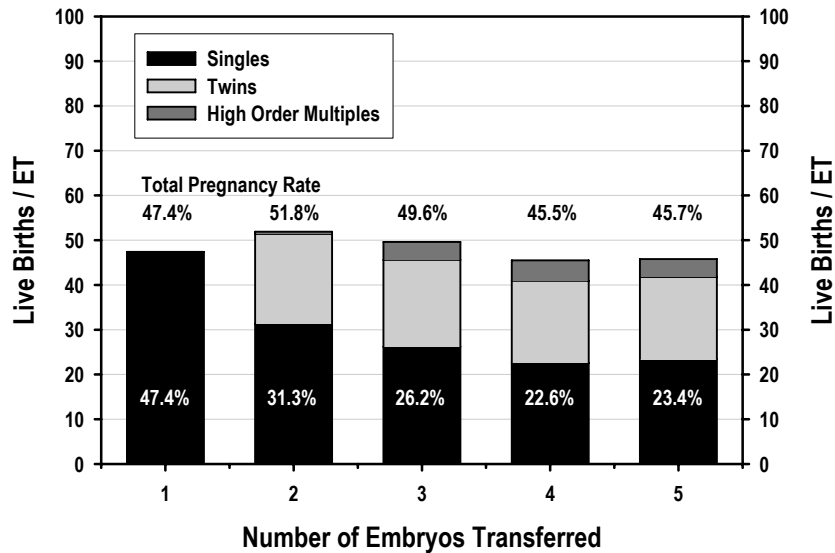
EGG RETRIEVAL AND EMBRYO TRANSFER

We retrieve the eggs from the donor and combine them with the sperm from the partner or donor sperm. Once the embryos form we transfer some of them into the endometrial cavity either 3 or 5 days after egg retrieval. The embryo transfer process for donor eggs is the same as for conventional IVF.

The success rate with donor eggs is so high that we must be very cautious about the number of embryos transferred to avoid the risk of high order

multiple (HOM) births (triplets or greater). We suggest that you anticipate transferring only 2 embryos unless we find that the embryos are unexpectedly lower in quality. Indeed, under selected conditions, transferring a single embryo may be the best treatment decision.

Note that transferring larger number of embryos does not increase the probability of pregnancy but does increase the probability of multiple gestations and HOM pregnancies. This data comes from non-donor IVF when excess embryos are available for transfer which is similar to a donor egg cycle. Unfortunately, the CDC data does not provide the same breakout for donor eggs as for non-donors eggs but this graph illustrates the point well.



Data from 2002 CDC SART National Success rates, Non-Donor Egg (used as an example)

RECIPIENT CONTROLLED ENDOMETRIAL DEVELOPMENT (CED) - CONTINUED

After the embryo transfer, the recipient needs to continue her hormone replacement because she does not produce any natural hormones from the ovaries. If she were to stop the hormone replacement, the pregnancy would die because the ovaries produce all the hormones necessary to stimulate the endometrium and sustain a pregnancy for about 7 weeks after ovulation. At about 7 weeks after ovulation or egg retrieval, the pregnancy produces enough hormones itself to be self-sufficient. As a precaution, we continue the hormone replacement until 10 weeks of pregnancy to ensure that the placenta is fully functional.

PREGNANCY OUTCOMES

Pregnancies from donor eggs generally have similar outcomes to naturally conceived pregnancies with the exception of a higher incidence of multiple gestations and their attendant risks. (1-3)

A number of studies have looked into the childhood development and family life after donor gametes were used to produce the pregnancy. Donor egg babies and parents have the similar outcomes to naturally conceived children. (4-7)

PSYCHOLOGICAL SUPPORT

Some couples choose donor egg IVF without any apparent stress. Nevertheless, many recipients experience some difficulty with the process of letting go of using their own eggs and moving on the using the eggs of another women. Some recipients, never become comfortable with using donor eggs.

We offer a mind-body program aimed at reducing general stress and improving the whole person. In addition, we can refer those who need assistance with the concept of using donor eggs or those who need assistance with the grieving process of losing one's natural fertility to a trained mental health professional. Our purpose to offer donor egg IVF to those recipients who have a deep comfort level with it.



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