Age Related Fertility
Preservation: Should you
Consider Multiple Egg
Freezing Cycles?

### Age Related fertility Preservation:

## Should you Consider Multiple Egg Freezing Cycles?

All what we really know for sure about reproductive competence (ability of eggs and sperm to produce a baby) is that embryos that has the correct number of chromosomes has a very high chance of implanting and produce healthy babies. In the majority of cases, the egg is the source of abnormal chromosome material: extra or missing chromosomes.

Female age is the most important fertility factor. As age advances, the number of eggs in the ovary decline and the proportion of abnormal eggs increase. This fact underline the need for modern women think about *reproductive planning* as early as possible, say age 25 to 30. When do you want to get pregnant for the first time? Is it socially feasible to start now? Do you have enough support around you to have a baby now? how large of a family do you want? do you care about the sex of the baby?

In general the following are available options

Try to get pregnant on your own as early as possibly can

Consider Embryo freezing with partner for later use

Consider using donor sperm to create embryos for storage

Egg freezing is a viable option for fertility extension

### Egg Freezing

The ovaries are stimulated to produce multiple eggs. Eggs are retrieved using a simple procedure. Mature eggs are frozen using flash freezing (vitrification). The eggs are stored in a special device in liquid nitrogen, indefinitely. The main aim here is to freeze multiple mature eggs at a younger age that can be used at a later female age when eggs are fewer and less healthy.

The most critical part of counseling women here about ultimate chance of conception using egg freezing is accurate estimation of egg reserve via <a href="https://doi.org/10.1001/journal.com/">history, antral follicle count and AMH level</a>.

In general women <38years that produce >8 eggs has a very good chance of conceiving and delivering at least one baby from an egg freezing cycle.

#### Egg-freezing-study

Women who are older or produce less eggs then would ask do I need more eggs?

### **Multiple Egg Freezing Cycles**

Should you Consider Multiple Egg Freezing Cycles? If you do not produce enough eggs in the first round of egg freezing you can consider another egg freezing cycle. But you now have the advantage of knowing how did you respond the first round. You know a bit more about the quality and maturity of the eggs. You know if the stimulation protocol worked for you and you can discuss with your reproductive endocrinologist methods of improving response. If increasing the number of frozen mature eggs is possible with another cycle of egg freezing, then another cycle should be considered.

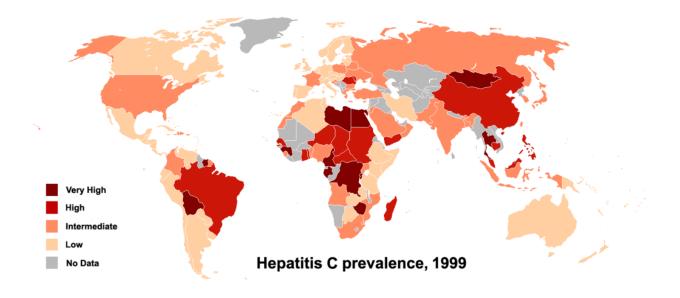
On the other hand if the prior response is low, egg quality is low and age is 40 or more, women should consider conceiving as soon as possible.

# Hepatitis C: what do you need to know if trying to conceive

## Hepatitis C: what do you need to know if trying to conceive

### **Hepatitis C Infection**

Hepatitis C Virus (HCV) infects 3% of the world's population. Over 170 million chronic carriers. Approximately 2.7 million Americans (1.8%) are infected with HCV in addition to 30,000 new cases reported yearly. In the United States, 65% of persons with HCV infection are aged 30-49 years. There are several types of the virus that vary in geographical distribution and response to medications.



Genotype 1a occurs in 50-60% of patients in the United States. Genotype 1b occurs in 15-20% of patients in the United States; this type is most prevalent in Europe, Turkey, and Japan. Genotype 1c occurs in less than 1% of patients in the United States

Genotypes 2a, 2b, and 2c occur in 10-15% of patients in the United States; are widely distributed and are most responsive to medication

Genotypes 3a and 3b occur in 4-6% of patients in the United States; most prevalent in India, Pakistan, Thailand, Australia, and Scotland

Genotype 4 occurs in less than 5% of patients in the United States; it is most prevalent in the Middle East and Africa

Genotype 5 occurs in less than 5% of patients in the United States; it is most prevalent in South Africa

Genotype 6 occurs in less than 5% of patients in the United States; it is most prevalent in Southeast Asia, particularly Hong Kong and Macao

Transfusion of blood contaminated with HCV was once an important source of transmission. Since 1990. Persons who inject illegal drugs with non-sterile needles or who snort cocaine with shared straws are at now at the highest risk for HCV infection.

Transmission of HCV to health care workers may occur via needle-stick injuries or other occupational exposures. Nosocomial patient-to-patient transmission may occur by means of a contaminated colonoscope, via dialysis, or during surgery, including organ transplantation before 1992.

HCV may also be transmitted via tattooing, sharing razors, and acupuncture. The use of disposable needles for acupuncture, which has become standard practice in the United States,

eliminates this transmission route. Other uncommon routes of transmission of HCV, which affect less than 5% of the individuals at risk, include high-risk sexual activity and maternal-fetal transmission. 10% unknown.

Tests for detecting hepatitis C virus (HCV) infection include:

- Hepatitis C antibody testing
- Recombinant immunoblot assay
- Qualitative and quantitative assays for HCV RNA
- HCV genotyping

#### **Hepatitis C Treatment**

Significant progress in the treatment of hepatitis C infection took place in the past year. Several medications or combinations can lead to cure in about 10 weeks in the majority of hepatitis C infected patients. Medications include Sovaldi (sofosbuvir 400 mg), Harvoni (ledipasvir (90 mg)/sofosbuvir 400 mg) or Vikera pak, with or without ribaverin.

One treatment regimen is a single daily tablet of ledipasvir 90mg / sofosbuvir 400mg for 8 to 24 weeks (according to genotype, viral load and functional status of the liver).

#### Hepatitis C and Reproduction

Significant effort is excreted by reproductive endocrinologist to detect hepatitis C and other viral infections and to prevent the transmission of hepatitis C to women and babies during reproduction.

Intimate partners: both partners are screened for HCV antibodies. If one partner is infected, he or she is referred for treatment with one of the modern drug regimens for 8 to 12 weeks before fertility treatment. If viral load does not drop to an undetectable level then a protocol exists for infected men to test semen for the virus and use the frozen sperm for IVF and ICSI to minimize transmission to mother and baby.

Egg and sperm donors: extensive history, exam and screening for donors is performed. Those with high risk factors are excluded. Donors with no risk factors are further tested using hepatitis C antibody and hepatitis C RNA performed in an FDA approved lab. Sperm donors are tested before sperm donation, sperm are quarantined for 6 months and the donor is retested again before releasing sperm. Egg donors are tested in an FDA approved lab within one month of egg retrieval. So far, there is no reported case of hepatitis C transmission after sperm or egg donation.

Gestational carriers: Intended parents are screened in an FDA lab for viral infections to minimize transmission to surrogates. Gestational carriers are also screened to prevent transmission to the baby.

Frozen sperm, eggs and embryos: liquid nitrogen in storage tanks can very rarely transmit infection. All patients are screened before storage. Tissues and cells can be stored in nitrogen vapor and sealed devices. Liquid nitrogen can also be filtered and sterilized using ultraviolet rays.

# What Does Borderline Ovarian Tumor Mean to Your Fertility?

## What Does Borderline Ovarian Tumor Mean to Your Fertility?

Fertility in women diagnosed with borderline ovarian tumors can be reduced or lost due to surgical treatment. Counseling regarding fertility preservation shortly after diagnosis can increase the chance of pregnancy following treatment.

### Borderline-low malignant potential ■ ovarian tumors

The cells in borderline tumors, proliferate more than benign ovarian cysts but less than frank malignant ovarian tumors. Multiple layers of these cells are seen on pathology slides, but they do not invade surrounding tissues as in malignant tumors. They are diagnosed in approximately4000 of women each year in the US and are more commonly encountered in reproductive age women. These tumors are usually cystic, sometimes with surrounding implants. Low malignant potential tumors are treated surgically (removal of cyst, removal of the ovary or sometimes removal of both ovaries and the uterus). They generally do not require chemotherapy for treatment. The majority of these tumors are associated with very high survival (10 year survival >90% in stage I and II ), although some may recur or turn malignant.

There is no difference in survival if borderline tumors were treated with removal of the cyst, removal of the ovary or removal of the uterus and both ovaries. Recurrence may be lower after hysterectomy (5%) compared to salpingoophorectomy (15%) and cyst excision (30%). The high rate for recurrence after conservative surgery indicates the need for strict and long term follow up (pelvic exams, ultrasound and tumor markers). Some recurrences take place years after initial surgery and are sometimes malignant.

### Fertility risks in women diagnosed with borderline tumors

Fertility risks in women diagnosed with low malignant potential ovarian tumors include loss of ovarian tissue and pelvic scarring that can block the fallopian tubes especially if open approach is used for treatment compared to laparoscopy (minimal acess surgery). Some loss of ovarian tissue does occur even during cyst removal from the ovary. Ovarian reserve can be tested after surgery using transvaginal ultrasound evaluation for ovarian volume and number of antral follicles. Ovarian function can also be assessed using day 2 FSH and estradiol levels and antimullerian hormone (AMH).

# Fertility preservation strategies in women diagnosed with borderline ovarian tumors

#### 1. Conservative surgery

Ovarian cystectomy can be considered in reproductive age women, especially in early disease with favorable pathology and absence of implants. Recurrence is relatively high but can be managed with repeat excision if not malignant. If pregnancy is desired following surgery, fertility factors; ovulation, fallopian tubes and sperm factors should be investigated and treated accordingly

#### 2. Embryo and oocyte cryopreservation

Women at risk for diminished fertility due to surgery, especially if requiring removal of the ovaries or repeat excision of cyst, can consider ovarian stimulation, egg retrieval and egg freezing or IVF and embryo freezing. There is no evidence that ovarian stimulation and exposure to high estrogen increases the risk for recurrence. It is not clear if border line cells are sensitive to estrogen increase during ovarian stimulation. Two options are available to reduce estrogen exposure: to perform IVF in a natural cycle (low egg yield) or to modify the stimulation protocol, through adding an aromatase inhibitor, similar to that used for breast cancer. Alternatively, short stimulation followed by retrieval of immature eggs followed by in vitro maturation can be performed.

Women diagnosed with borderline ovarian tumors are at risk for diminished fertility because of surgical treatment(s). This is especially true if repeat surgical excision is required. Collaboration between a gynecologic oncologist and a reproductive endocrinologist enable adequate surgical treatment, strict follow up and preservation of future fertility in reproductive age women.

## Egg Freezing what Do you Hope to Accomplish?

### Egg Freezing what Do you Hope to Accomplish?

The best approach motherhood is to actually try to get pregnant. Though methods of fertility preservation are very helpful, none is a guarantee to make a baby in the future. So the primary advice is "try to get pregnant if you can" after checking different fertility factors (male, tubal and ovarian factors as well preconception screening). If getting pregnant is not feasible in the short term, due to medical or social issues, egg freezing is considered. A reproductive endocrinologist is faced with the challenge of foreseeing if a specific woman, when stimulated and her eggs are harvested and frozen, has a reasonable potential to conceive using these eggs at one time in the future.

### Indication for Egg Freezing

Women should consider <u>egg freezing</u> when specific medical or age related situations threatens their ability to have a child

in the future.

- 1. Fertility preservation: When a medical disorder or its treatment can diminish ovarian reserve and reduce the chance for conception e.g cancer treatment (most common is breast cancer), lupus nephritis requiring treatment with chemotherapy, blood diseases requiring bone marrow transplantation, premature ovarian dysfunction and others. About 2 weeks should be available for an egg freezing cycle.
- 2. Fertility extension (no male partner): women with no male partner and declining the use of donor sperm can freeze their eggs to use in the future when in a committed relationship.
- 3. Fertility extension (with a male partner): women with a male partner can elect to freeze some of their eggs unfertilized. Unfertilized eggs are under the control of the woman alone, unlike embryos that cannot be used without the consent of both partners.
- 4. IVF with failed sperm retrieval or ejaculation: In some cases with male factor with failed retrieval of sperm from the testes or failed ejaculation, eggs can be frozen and used later when sperm are available.
- 5. Children undergoing treatment for cancer and other diseases with the ascent of their parents.

### What should you consider before proceeding to egg freezing

i. Women <38 years with good ovarian reserve: are excellent candidates for egg freezing. Good reserve is indicated by antral follicle count >10 as seen on vaginal ultrasound and AMH levels > 1.75 ng/mL. They will likely produce a good number of oocytes to freeze in a single cycle. These eggs are relatively healthy as they are young. Age <36 years was the best predictor of egg freezing so far in scientific reports.

- ii. Women <38 years with diminished ovarian reserve: are still good candidates for egg freezing. They produce lower number of eggs after stimulation but their oocytes are relatively healthy (chromosomally normal). They can undergo more than one cycle of egg freezing if the first cycle yields <8 mature eggs.
- iii. Women 38-40 years with good reserve: can still consider egg freezing with no further delay.
- vi. Women 38-40 years with diminished ovarian reserve: should consider egg freezing with caution. They will not produce a good number of eggs and may require multiple cycles of egg freezing.
- V. Women >41y are not good candidates for egg freezing even if they have a good reserve as the majority of their oocytes are not chromosomally normal. Although pregnancies were reported from vitrified oocytes up to age 44, the chance of pregnancy in quite low in women older than 40.

#### Realistic Expectations for egg freezing

Not only should the number and quality of eggs be considered, but also the survival of thawed eggs, fertilization and ultimate ability to implant. These issues are very sensitive to the method of ovarian freezing. Vitrification (rapid freezing) is not the method of choice for low temperature storage of eggs due to high survival and subsequently fertilization and embryo development (more details here and here).

Survival on average 85% of virified thawed eggs survive, irrespective of age.

Fertilization approximately 80% of thawed eggs fertilize after injecting each with a sperm (ICSI).

Age specific chance for a live birth after thawing of

vitrified eggs can be presented in different ways. The delivery rate is approximately 5 to 15% per thawed egg depending upon the female age at freezing. For example, if eggs are thawed and fertilized and three embryos were transferred to the uterus, the probability of delivery would be 25% at age 30 and 15% at age 40.

If a 35 year old decided to proceed with an egg freezing cycle and produced 10 eggs, 8 eggs were mature and frozen. When she present back 10 years later to utilize her eggs and thaw all of them 7 eggs are expected to survive, 6 eggs are expected to fertilize. If three embryos were transferred her chance for delivering a baby is 20% (the remaining three embryos are frozen). If The first cycle does not succeed and the next three embryos were transferred, her cumulative chance for having a baby from the original egg freezing cycle is approximately 40%.

Sorting through statistics of egg freezing is difficult. No single clinic can present convincing statistic due to small number of egg thaw and transfer (not just egg freezing cycles). Most studies present select donors and selected women and not directly applicable to everyone. And then there is the safety issue and lack of long term follow up data related to safety and health of newborns.

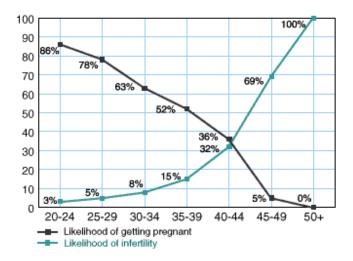
Age is most important predictive of success of egg freezing followed by method of freezing. Vitrification much better than older slow freezing methods. There is now reasonable body of data, though not definitive, that allows prediction of outcome for egg freezing using vitrification based on age and the expected number of retrieved oocytes. It is neither accurate nor scientific to label egg freezing with terms such as reliable and guarantee. It certainly is not a guarantee of children. What is more productive is to i. try to avoid egg freezing through trying to conceive. If not possible, in a short while, then ii. understand your own personal chances of delivering a healthy baby through egg freezing and if they

seem reasonable to you consider the procedure, taking in consideration the limitation of available data and filtering out the marketing hype.

## <u>Fertility Options for Single</u> Women

### Fertility Options for Single Women

Single women may face some challenges regarding fertility options: understanding them then picking one or more options, suitable for your reproductive plans. Clearly, a woman cannot delay pregnancy indefinitely, as the number of good quality eggs decline quickly in her 30s and older.



Decline in Fertility with age

Modern reproductive medicine enables single women to be mothers now and in the future. As with anything in

reproduction, the younger you are, the more successful your efforts will ultimately be, irrespective of your choices. In addition, think of what would you accept: donor sperm? are you ready to get pregnant now or do you want do that in the future?

### Are you ready to Start a Family without a Partner?

This could be a difficult question considering the time, financial and emotional commitment of raising children without a male partner. A psychologist with expertise in reproductive issues can help women tackle issues as readiness and commitment, disclosure to children when mature, capitalizing on family resources, legal issues and many more. Some anonymous donors accept open identity in the future.

Starting a family without a male partner requires a selection of sperm donor. The sperm donor could be anonymous (from a sperm bank) or known (friend). In either cases, the donor is screened for infectious diseases (hepatitis B, hepatitis C, HIV, Syphilis, Gonorrhea and Chlamydia) and common genetic abnormalities. The sperm is quarantined then the donor is retested for infectious diseases. Tests are done in a specialized high accuracy labs.

#### How to use donor sperm to achieve a pregnancy?

This is a question related to female ovarian reserve and other fertility factors. If the fallopian tubes are open, as indicated by HSG (hysterosalpingogram, X-ray of the tubes) then IUI (intrauterine insemination) is possible. Age is also an important factor. Women 38 or older have much higher chance of conceiving with IVF than IUI using frozen sperm. This issue require thorough evaluation by a reproductive endocrinologist.

#### On Starting a Family with a Partner in the Future

If the use of donor sperm is not acceptable, <a href="egg freezing">egg freezing</a> is a viable option for women with reasonable ovarian reserve and

younger than 40. Evaluation of antral follicle count using vaginal ultrasound and antimullerian hormone levels (AMH) can predict response to fertility medications and ultimate egg yield from the cycle. Age reflects well how many of these eggs are chromosomally normal. The ovaries are stimulated using injection medications. Eggs are retrieved under vaginal ultrasound guidance which is a minor procedure. Mature eggs are frozen 4 hours later using vitrification. Immature eggs are cultured for <24 hours and frozen if mature. The eggs can be stored for years to come.

If the number of eggs retrieved is low another egg freezing cycle can be attempted to freeze more eggs.

When pregnancy is desired the eggs are thawed and fertilized via ICSI (direct injection of the sperm into the egg) and the resulting embryos are transferred into the uterus after preparation of its lining. The pregnancy rate after egg freezing is close to fresh eggs and is age dependent.

These options allow single women achieve their reproductive goals while respecting their values and preferences.

## What Can you Accomplish through IVF ?

Defining your reproductive goals early on before starting is essential in guiding the choice of treatment. <a href="IVF">IVF</a> is the most versatile and robust fertility treatment available. In addition, it accomplish many reproductive goals that are no achievable with IUI.

### What Can you Accomplish through IVF?

### Getting pregnant now

IVF can be performed in almost all causes of infertility:

Ovarian factor, male factor, tubal factor, emndometriosis, polycystic ovary syndrome (PCOS) and uterine factor. Success does not appear to be affected by the cause of infertility with the exception of diminished ovarian reserve. Hence, it is important that you seek evaluation as early as you can.

The ovary is stimulated using fertility medication. Various protocols of treatment are tweaked to your special situation and to maximize egg production. Sometimes mild or minimal stimulation IVF is a more suitable approach. Eggs are retrieved and fertilized in the lab using husband or donor sperm.

Embryos are graded based on morphology (shape) and an appropriate number is transferred into the uterine cavity. In the majority of men, sperm is obtained from the ejaculated sperm. In some surgical sperm retrieval (TESE) is required.

### Getting pregnant with a single baby

Conceiving with a single baby should be the aim of every woman. The risk of twins and high order multiple pregnancy is high risk of preterm delivery. Premature delivery can lead to long term health problems in the babies. Unlike IUI where the number of embryos reaching the uterine cavity cannot be controlled, IVF allows for a strict control on the number of embryos reaching the uterus. Women with reasonable quality embryos up to age 38 or so can consider the transfer of a single embryo and freezing the other embryos.

In that regards IVF is the more conservative approach when

compared to IUI, besides being several folds more successful in achieving a pregnancy.

### Getting pregnant in the future with a current partner

Embryos created now after IVF, can be frozen for several years. When desired, frozen embryos are thawed and transferred into the uterus in a natural or hormone treated uterus. This allow you to extend your fertility for years to come. The survival of frozen embryos is excellent, especially using moder freezing methods (vitrification).

The pregnancy rate after transfer of frozen embryos is comparable to fresh embryos. There is also some evidence that pregnancies ensuing after transfer of thawed embryos are at lower risk for obstetrical problems.

### Getting pregnant in the future with a future partner

If you do not have a male partner and do not want to use donor sperm, you can consider freezing your eggs. Because your ovarian reserve; the number and quality of eggs; will diminish as the time goes by, freezing eggs at an earlier age, enables you to freeze healthier eggs and use them years later when you are ready. Egg freezing is a fertility solution for fertile women.

### Selecting the Sex of the Baby (Family Balancing)

Eggs are retrieved, fertilized. The resulting embryos are tested; one cell is obtained from each embryo and tested for the X and Y chromosomes to identify the genetic sex. The desired embryos are transferred into the uterus . Women consider sex selection for family balancing (had a baby of one

sex and desire another baby of the other sex). Women consider sex selection when they want to reach their reproductive goals e.g one boy and one girl, while limiting the number of children conceived.

### Getting Pregnant with Donor Eggs

For women with markedly diminished egg reserve or some genetic abnormalities, using an egg donor is an option. Egg donor may be known or anonymous. The donor is stimulated and fertilized with partner or donor sperm then the embryos are transferred to the uterus of the mother or a gestational carrier.

### Becoming a Biological Parent without Getting Pregnant

Some women are not able to get pregnant in their own uteri because of a condition affecting the uterus: scarring, multiple fibroids, adenomyosis, recurrent preterm delivery..Others prefer not to get pregnant because of a general health problem: successful treatment of breast cancer, severe hypertension or heart disease. Embryos are created through IVF and transferred to the uterus of a gestational carrier (surrogate mother).

### Genetically Test the embryos before getting pregnant

Embryos created after IVF can be tested genetically for i. A specific gene or ii all the chromosmes. This is accomplished through two steps. Biopsy of the embryos (one cell in day 3 embryos or few cells from the trophoectoderm of day 5 embryos — blastocysts). The cells are tested for the desired genetic target and the healthy embryos are transferred to the uterus.

### Becoming a Biological Father if you are in a Same Sex Relationship

Men in a same sex relationship can father children using an egg donor and a gestational carrier. The donor ovaries are stimulated. Eggs are retrieved and fertilized with one partner sperm or split between partners. Embryos are then transferred into the uterus of a gestational carrier.

### Preserve your Fertility in the face of a medical Problem

Sometimes a a medical problem or its treatment reduces the chance for future reproduction. Breast cancer treatment in young women commonly involve treatment with chemotherapy. Medical problems other than cancer also may require treatment with chemotherapy e.g systemic lupus. Chemotherapy leads to loss of ovarian follicles and diminish egg reserve.

The ovaries are stimulated prior to exposure to chemotherapy. Oocytes are retrieved and frozen unfertilized or after fertilization. After treatment, eggs or embryos can be thawed and used for reproduction.

### How Successful is IVF ?

Irrespective of the situation, the most important factor in <a href="IVF success">IVF success</a> is the number and quality of eggs remaining in the ovary (Ovarian reserve). Maternal age is the most important determinant of egg reserve. Younger women have more chromosomally normal eggs and are more likely to have a baby after IVF.

In women younger than 35, the transfer of two embryos yields a pregnancy rate of 48 to 50% and one embryo 35 to 40%. In women 40 or older the pregnancy rate per cycle is approximately 5 to 20% depending on age. Many cycles in older women are not

completed due to low response to fertility medications.

Modern IVF enables many women and men to achieve there reproductive goals and conform to their social and personal preferences and aspirations.

### **Egg Reserve and Infertility**

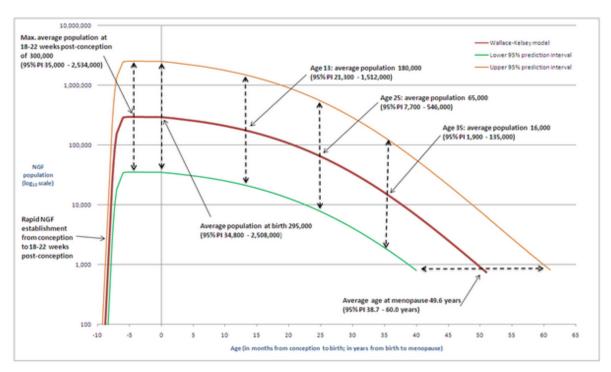
Egg reserve means the number and quality of eggs remaining in the ovaries at a given age. It reflects the fertility potential of a woman irrespective of the cause of infertility, even male factor.

### Benefits of Testing for Egg Reserve

Testing for egg reserve results should be interpreted with caution. Abnormal values should not be a cause for denying fertility treatment because the predictive power for pregnancy with own eggs is modest. For women, ovarian reserve tests give women insight into the chance of pregnancy with there own eggs. It also may indicate the need to promptly avoid delay in seeking fertility treatment. For reproductive endocrinologists, the tests have value in designing fertility treatment and selecting the most appropriate fertility treatment protocol. They predict response to fertility medications and allow infertility specialists to select treatment protocol and gonadotropin dose. Egg reserve also predicts the number of eggs retrieved for IVF or egg freezing.

### Egg Reserve: Egg Number

Although the number of eggs in the ovaries decrease with age there is significant individual variation in initial number endowed in the ovaries and the rate of decrease. Some young women has low egg number and older with large number of eggs. Ovarian reserve tests are used to estimate this number.



Egge reserve: the number of eggs in the ovaries drops with age

### **History**

Medical history may indicate low egg reserve in women with prior excision of ovarian cysts, endometriosis of the ovaries, women who smoke and with family history of early menopause

### Antral follicle count

The number of antral follicles in the ovaries (the structures that contain the eggs) can be seen and counted using vaginal ultrasound. Performed by an experienced reproductive endocrinologist, it can accurately estimate ovarian reserve. Low count e.g <10 in both ovaries points to low reserve.

### Day 3 FSH, Estradiol

FSH is produced by the master gland in the base of the brain. Estradiol is made by the follicles themselves. Measured in the second or third day of menstrual cycle, high FSH (>12) of high estradiol (>75) points to low egg reserve.

### **Antimullerian Hormone (AMH)**

AMH is produced by the cells surrounding the eggs in small follicles and is a more direct measure of egg reserve than FSH. It can be accurately measured any day in the cycle with little variations in between cycles. Levels <1.5 ng/dL generally indicates low egg reserve. It correlates well with antral follicle count.

### **Genetic Screening**

Low egg reserve in few women is due to a genetic cause. Fragile X syndrome is a genetic disease that causes low egg reserve and mental deficiency in newborn males. Chromosomal abnormalities e.g Turner syndrome, translocations are also associated with low egg reserve. Genetic screening is performed using a simple blood test before starting fertility treatment.

### Egg Reserve: Egg Quality

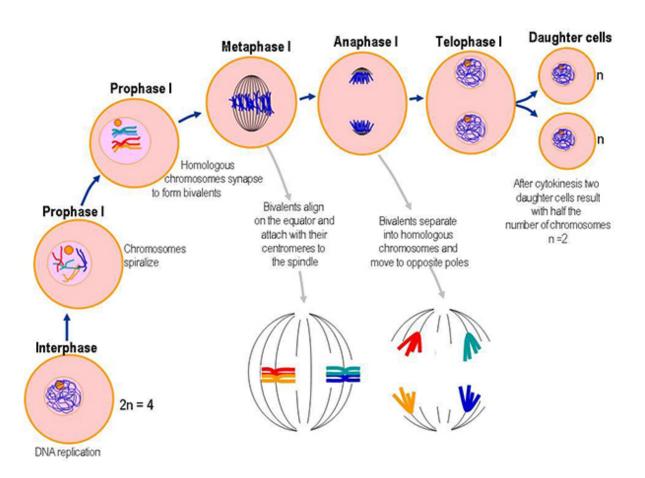
### What does egg quality means ?

Good quality eggs are chromosomaly normal (has 23 chromosomes). The most important factor that prevents the achievement of pregnancy or leads to early miscarriage is an abnormal egg (has extra or missing chromosome or piece of a chromosome). Many eggs at any age in any woman are abnormal and the normal eggs are the ones that are successful in being fertilized with sperm, implant and achieve a pregnancy. These

errors takes place when the original cell that produce the eggs divide to reduce the number of chromosomes to half. The division (meiosis) is many times unequal leading to an egg with an extra or missing chromosome.

### Age and egg quality

The ovary releases better quality age earlier in life and lower quality age later, for unknown reason. Female age is the most important indicator for egg quality, chance for spontaneous pregnancy and after fertility treatment. Older women need to try longer to achieve pregnancy and at an increased risk for miscarriage, ectopic pregnancy and delivering a baby with chromosomal abnormalities e.g Down Syndrome. This effect of age become clinically evident at age 30 or even earlier. Age is more important than the number of eggs in the ovaries. Young women with few eggs in the ovary are more successful in getting pregnant than older women with many eggs in the ovary.



### Testing for egg quality: PGD

Age is the only available noninvasive method to estimate egg quality. Healthy eggs cannot be identified using any non invasive method. It is possible to identify chromosomal errors in the egg during IVF fertility treatment after biopsy of the first polar body of unfertilized egg or after removing one cell from an embryo after the egg is fertilized then test this material for chromosomal abnormality. This process is called PGD or preimplantation genetic diagnosis. It is important to remember that PGD is not proven so far as method of enhancing fertility potential. It simply detects if the egg or embryo is chromosomaly normal or not but will not make an unhealthy egg healthy.

Read more about ovarian reserve and low response to ovarian stimulation in my review <a href="here">here</a>.

### **Egg Freezing**

### Women freeze their eggs for one of two reasons

- 1. Elective: **freezing eggs** to use later on to avoid age related decrease in egg quality and number. This is a fertility solution for fertile women.
- 2. Medical indication: women diagnosed with cancer and require surgery or chemotherapy that will reduce ovarian function, egg donation and egg banking, failure of the the male to produce sperm at the time of IVF.

### Is egg freezing suitable for me?

You need *personalized information* about ovarian reserve and reproductive system before deciding on egg freezing. <u>Ovarian reserve</u> is an estimate of the number of eggs in the ovary and their quality. The number of eggs is estimated using vaginal ultrasound for antral follicle count, AMH levels and day 2 or 3 FSH and estradiol. AMH levels > 1.5ng/dL and antral follicle count > 12 indicate decent number of eggs in the ovaries.

Egg quality is reflected by age. The younger the age, the more chromosomally normal eggs are available in the ovary.

Women 38 or younger freezing more than 8 eggs have excellent chance to become pregnant when eggs are thawed, fertilized and transferred to the womb. Live birth rates decline with age but some live births took place from eggs frozen up to age 44.

Approximately 90% of eggs stored using vitrification survive thawing and 75% of them fertilize. Each egg thawed has the potential to produce a baby approximately 10% of the time (5 to 15% depending on age). Commonly, three to four eggs are thawed and two to three embryos are transferred. This will yield a reasonable live birth rate per cycle. The American Society For Reproductive Medicine does not consider egg freezing an experimental technology anymore.

#### What do I need do to freeze my Eggs?

Ovarian stimulation: using injection medications to recruit multiple follicles and produce multiple eggs, instead of one egg only in a natural cycle. Medicine is self injected daily for approximately 10 days and monitored using estrogen levels and ultrasound every two to three days. A trigger injection is finally given.

Egg retrieval: eggs are harvested under sedation 36 hours after the trigger injection. **Eggs** are obtained using a needle through the vagina without an incision.

Egg freezing: Vitrification method is used. Four hours after retrieval, Mature eggs are mixed with a cryo-protecting solution. Two to three eggs are placed on a special device cryotop that is sealed and plunged in liquid nitrogen or nitrogen vapor. Immature eggs can also be frozen.

The cycle can be repeated. Also some of the eggs can be fertilized using donor sperm if desired.

#### What happens after I freeze my eggs?

Frozen eggs Can be stored for a very long time, possibly indefinitely. Eggs can also be transferred to other facilities or countries.

When you are ready, with a partner: try natural conception, investigate other fertility factors, consider fertility treatment or finally use the eggs.

When you are ready, without a partner: try IUI using donor sperm or IVF using donor sperm or fertilize the frozen eggs with donor sperm.

Utilizing your **frozen eggs**: The steps to utilize your eggs are

- 1. Preparation of the lining of the uterus using estrogen (no injections) or during your natural cycle,
- 2. Egg thawing in the embryology lab,
- 3. ICSI: injection of one sperm into each egg,
- 4. Embryo development and transfer is observed in the lab
- 5. Transfer of one or more embryos into the uterus

### Is egg freezing safe?

Babies born after thawing the eggs, fertilization and transfer into the uterus do not have higher risk of abnormalities compared to those born from after transfer of thawed embryos or naturally conceived. However, there has not been as much babies born using this technology or long term follow up as in

the case of embryo freezing.

#### Conclusion

If you did not attempt to conceive by age 30 or earlier, consider evaluation of ovarian reserve and egg freezing if you do not intend to get pregnant soon. Obtaining personalized information about egg reserve is the primary step in deciding if egg freezing is suitable for you.

### **Endometriosis & Infertility**

Endometriosis & infertility commonly coexist. Endometriosis can have profound effects on woman's fertility and the ability to conceive in the future, either by virtue of the disease itself or its treatment. Endometriosis means that the tissue that lines the uterus is found in other areas, most notably the ovaries and the lining of the pelvis, frequently causing pelvic pain and infertility. In early stages of endometriosis, the implants in the pelvis may chemically affect various stages of reproduction including fertilization and implantation. In later stages, endometriosis incites scarring that can block the fallopian tubes and can produce cysts in the ovaries called endomertiomas. Experienced reproductive endocrinologist can diagnose endometriomas with high degree of accuracy using ultrasound. In other areas the diagnosis of endometriosis may requires laparoscopy.

### Treatment of Endometriosis

Women seek treatment for endometriosis because of pain or infertility. Treatment for endometriosis is either medical or

#### Medical treatment For Endometriosis

It entails suppression of ovulation and estrogen production. Estrogen stimulates the growth of endometriosis. Medical treatment has side effects and is not suitable for women seeking pregnancy now. It, however, does not have a long lasting effects on fertility. Medications used include oral contraceptive pills, androgenic medications or gonadotropin releasing hormone agonists as depot leuprolide. Women on these medications does not need to consider fertility preservation strategies because of treatment.

### Surgical Treatment For Endometriosis

Surgery aims at removal of endometriosis spots in the pelvis or excising endometrioma cysts from the ovary. Cutting the ovary and stripping the wall of the endometriomas is associated with loss of eggs during the procedure. The ovary, where the procedure is done commonly have <a href="less reserve">less reserve</a> and may show lower response to fertility medication. The risk for decreased fertility is higher if the procedure is done on both ovaries. It is also higher after extensive surgery, commonly associated severe disease in the pelvis. Sometimes the ovary need to be completely removed . Removal of endometriosis deposits in the pelvis-usually burning them using cautery-can also incite scarring that can block the fallopian tubes. Women undergoing surgery for endometriosis should consider fertility preservation. Aspiration of endometriomas is generally not a recommended treatment as they tend to recur and can cause infection.

### Fertility Treatment in Women with

### **Endometriosis**

Severe Endometriosis mechanically blocks the fallopian tubs due to scarring. IVF appears to be the best treatment option. Although endometriosis reduces the response to ovarian stimulation, it does not appear to reduce the pregnancy rates

Mild endometriosis does not distort the fallopian tubes. Two treatment options are available: laparoscopy with excision or burning of endometriosis or ovarian stimulation + IUI. Both can increase the chance for pregnancy but IUI is less invasive.

### Fertility Preservation strategies in women with endometriosis

Reproductive age women diagnosed with endometriosis and advised to undergo surgery by their physicians should inquire about the possible effects of surgery on future fertility and consider fertility preservation strategies. Strategies include embryo cryopreservation, egg freezing or ovarian tissue freezing.

### **Embryo cryopreservation**

Its the standard method for preservation of fertility. It requires stimulation of the ovaries using fertility medication for approximately 10 to 12 days, followed by egg retrieval. Eggs are fertilized using partner or husband sperm. The resulting embryos can be frozen indefinitely. One risk is that endometrioma cysts can get infected at the time of egg retrieval.

### Egg freezing

It can be used in women not in stable relationship and declining the used of donor sperm. It require ovarian stimulation. This is followed by retrieval and freezing. Eggs

are frozen using <u>vitrification</u>. Vitrification is associated with better survival after thawing than slow freezing. When desired, the eggs are thawed and fertilized using intracytoplasmic sperm injection-ICSI and the resulting embryos are transferred to the uterus.

### **Endometriosis and Ovarian Cancer**

It was noticed that women diagnosed with endometriosis has a small increase in the risk for certain rare types of ovarian cancer. Its essential that endometriomas in the ovary be thoroughly investigated using ultrasound and other imaging modalities and sometimes blood tests. Surgery may be needed to remove the cyst and submit it for pathological examination to exclude cancer.