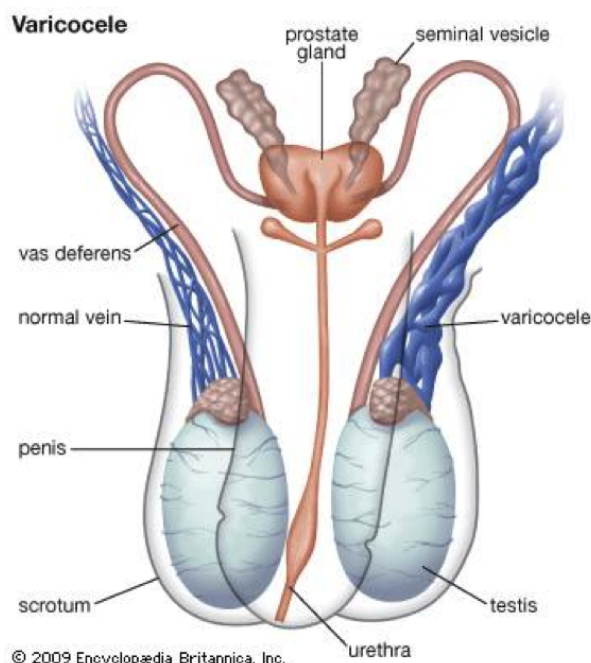


# Varicocele and Male Factor Infertility

## Varicocele and Male Factor Infertility

Varicocele and male factor infertility: Many men (40%) with low sperm count, low movement and high abnormal sperm shape have dilated veins around the testes. On the other hand, many men (15%) with varicoceles have normal sperm parameters and fertility. Only large varicoceles that can be felt by a physician are associated with lower fertility in men. Varicoceles are found during physical examination and can be confirmed with Doppler ultrasound of the testes. How dilated veins – varicoceles may cause abnormal sperm and [male infertility](#) is still unknown for sure (pressure, heat, toxin accumulation, oxidative stress).



varicocele surgery

# Does surgical treatment of varicocele increase the chance of pregnancy in female partners?

Some urologists recommends surgical treatment of varicoceles in adult men to improve the chance for spontaneous conception

This recommendation should at least be issued if and only if:

1. Varicocele was large enough to be felt on examination (not ultrasound).
2. The couple had documented infertility or desire future fertility.
3. The female partner had normal fertility (especially normal [egg reserve](#)) or correctable infertility.
4. The male partner had one or more abnormal semen parameters.

The rationale is that repair may restore normal sperm parameters and spontaneous conception. *Varicocele repair is definitely not indicated in the presence of female factor requiring IVF* e.g blocked fallopian tubes, as improved sperm parameters will not achieve a pregnancy. Some studies reported improved sperm parameters and sometimes fertility after surgical treatment of varicocele but many of them were low quality studies (no control group, not randomized, non-palpable varicocleles).

**Good quality studies:** randomized (one group of men underwent surgery for large varicoceles and another group did not)

Ten randomized studies were published (including 894 men). Some studies indicated improve in sperm parameters after surgery. Most of the studies indicated that the chance for live birth is not increased after varicocele repair. There is no conclusive evidence that varicocele repair increases the chance for pregnancy and delivery in female partners of men

diagnosed with varicocele (summary below).

**Surgery or embolization for varicoceles in subfertile men:**

**Varicocele is a dilatation (enlargement) of the veins along the spermatic cord (the cord suspending the testis) in the scrotum. Dilatation occurs when valves within the veins along the spermatic cord fail and allow retrograde blood flow, causing a backup of blood. The mechanisms by which varicocele might affect fertility have not yet been explained, and neither have the mechanisms by which surgical treatment of the varicocele might restore fertility. This review analysed 10 studies (894 participants) and found evidence (combined odds ratio was 1.47 (95% CI 1.05 to 2.05) to suggest an increase in pregnancy rates after varicocele treatment compared to no treatment in subfertile couples, in whom, apart from poor sperm quality, varicocele in the man was the only abnormal finding. This means that 17 men would need to be treated to achieve one additional pregnancy. However, findings were inconclusive as the quality of the available evidence was very low and more research is needed with live birth or pregnancy rate as the primary outcome (Kroese 2012).**

Surgical repair of varicocele should only be considered in carefully selected subfertile couples. There is no conclusive evidence that repair increases the chance for delivery in female partners. Data supporting surgical repair of varicocele are controversial and results of surgery is certainly inferior to IVF-ICSI.

A consultation with reproductive endocrinologist & fertility specialist is very important before deciding on varicocele surgery to study [female factor infertility](#) and discuss potential benefits and harm from surgery in achieving the final goal which is conceiving not just improving sperm count and motility.

[varicocele and Male Factor Infertility](#)

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# Money-Back Fertility Treatment Payment Plans

## *Money-Back Payment Plans*

Money-back fertility treatment payment plans or shared risk plans are payment plans that offer unsuccessful patients a portion of their money back. They usually include two or three fresh IVF cycles followed by the transfer of resulting frozen embryos. Money – back fertility plans commonly include fertility financing programs, fertility medication program and some re-arrange or restrict benefits through employer (sponsor) or insurance plan. All together called the bundle.

### **Who Qualifies for Money-Back Fertility Treatment Payment Plans?**

IVF programs that offer money back plans usually require certain age limits and normal to excellent ovarian reserve markers. Older women and those with low egg reserve usually do not qualify for such plans. Programs also place contingencies on ovarian reserve and transferring more embryos. Hence they exclude women interested in a single embryo transfer.

Some of the money – back fertility enterprise do not operate clinical IVF programs. They offer the financial scheme for payment and in some instances fertility drugs. They refer patients to clinics but do not conduct the treatment. The specifics of the couple may not coincide with the contingencies for money – back arrangement. The result is either you are alert to dismiss the plan or follow the plan and take your chances with the success rate. This is the most disturbing aspect of money-back fertility plans.

The delivery rates after fresh IVF in women commonly included in money back plans is close to 40% with single embryo transfer, 50% with two embryo transfer. Use of frozen embryos add approximately 30% chance for delivery after transfer of frozen embryos from the first fresh IVF cycle. In other words they are the least likely to require multiple cycles in the IVF population. Moreover, they are the most likely to get pregnant with multiple babies. The cost for money back fertility treatment plan is maybe higher than a single fresh IVF cycle and a transfer of frozen embryos. Interest is associated with monthly payment plans. Medicine and multiple treatment cycles are also sometimes bundled. In addition cost can escalate due to obstetric care for multiple pregnancy.

At New York City IVF we educate women and recommend single embryo transfer up to age 38.

One opinion about money back fertility treatment plans is [New York State Department of Health Task Force Report: Executive Summary on ART](#)

*Payment plans that offer unsuccessful patients a portion of their money back create significant ethical concerns.*

*Physicians whose payment depends on the success of treatment have an incentive to accept only those patients with a strong chance of success (perhaps patients who do not qualify as infertile under generally accepted standards) and to turn away needy patients whose outcome may be less certain. In addition, when payment is linked to outcome, physicians may encourage patients to accept aggressive treatments that increase the chance of success without due regard for the risk those treatments may entail.*

*Nonetheless, while the Task Force members are deeply troubled by the risks created by money-back payment plans, they do not believe that these plans are inherently unethical in all cases. Programs that offer money-back payment plans should*

*clearly inform patients of all essential terms of the plan. No plan should require patients to provide a blanket consent to all treatments and procedures recommended by their physician.*

*Patients enrolled in money-back payment plans should receive a prorated refund if they withdraw from treatment before they have completed all of the cycles covered under the plan. The most appropriate definition of "success" in the context of money-back payment plans is a live birth. The condition of the child should never be a factor in the definition of success*

IVF programs can address this ethical question using different arrangement. Reducing fees for the second cycle as opposed to selling multiple cycles together would be one suggestion.

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## **IVF: The Way We Do It**

### **IVF : The Way We Do It**

#### **Efficient approach**

IVF: The Way We Do It. We believe you should consistently be able to get an advice / recommendation for a fertility treatment, handcrafted to your special reproductive potential and egg reserve. *Your ovarian stimulation protocol will most certainly not be suited for the next woman.* We think carefully and for quite sometime about the best adjuvant and stimulation medication protocol, after obtaining adequate information about you and your partner. Moreover, attention to details

during stimulation avoids pitfalls and optimize the quality of oocytes through selecting the most appropriate size to trigger final egg maturation. We then present the regimen to you in a simplified and chronological presentation that is easy to follow.

We believe that you should be able to understand all the intricate details of treatment and train on medications within one to two visits (supplemented with phone calls and e mails). You and your reproductive endocrinologist can reach a treatment decision and even train you on execution parts of that decision in the second visit even if you did not do any fertility tests before. This is how we efficiently do it.

## **IVF : The Way We Do It**

### **I. Initial visit ultrasound, labs and prior records**

Basic information about you and your partner are collected through detailed history, exam and vaginal ultrasound. The main aim is to identify any specific fertility factor as well as estimate ovarian reserve. In addition we order fertility labs and preconception tests. We then discuss in details treatment options, including expected pregnancy rates, multiple pregnancy rates and potential complications.

We obtain and interpret lab results in few days and are discuss them with you especially genetic risk assessment, in person, via secure e mail or phone.

*Reproductive endocrinologists should want to care for their patients to help them acheive a healthy baby, not just go through the motions and dynamics of treatment, that has minimal or no chance of working. This is an absolute guiding and ethical principal. Its related to the biological possibilities detected on initial fertility testing and its also related to their physician skills and expertise. At the*

*end of the day infertility specialists need to be **clearly convinced** that a particular woman has a reasonable chance of get pregnant before initiating a proposed fertility treatment. Fertility specialists then should take that woman to her maximum potential.*

## **II. Second Visit: Saline sonography, trial transfer, medication teach, stimulation protocol.**

Checking the cavity of the uterus is essential to exclude factors that prevent implantation. Passing a catheter into the uterus helps anticipating difficulty in embryo transfer. Both are simple office procedures.

Ovarian stimulation Protocol Selection: we think deeply when assigning stimulation protocols in relation to dose and type of protocol (agonist or antagonist) and adjuvant use of medications before and during stimulation. Reviewing prior stimulation can help in improving the current protocol in terms of egg yield and quality. The physician that saw you first will conduct all day to day monitoring as well as all procedures. Attention to details during monitoring is paramount in determining the dose and length of stimulation and time for egg retrieval.

Additional procedures that we perform during an IVF cycle include sex selection, PGD, number of embryos for transfer, egg and embryo freezing are all available to you. I explain those in details.

Medication teach: a hands on exercise on using the medicine. Now You are ready to start.

## **III. IVF: monitoring, retrieval, embryology lab procedures.**

We always strive to deliver compassionate day to day Guidance, tailored around you comfort and convenience. We want you to waste minimal time waiting because you have the rest of your



life and work to attend to.

Cycle conduct: we meticulously interpret the response to stimulation through ultrasound and blood work, with each visit and modify the dose of medications to improve response in the ovaries and minimize complications. The same physician perform monitoring and daily instructions as well as all other procedures. He or she knows your story and you never have to repeat yourself to a new person each time.

Embryology procedures: egg retrieval and embryo transfer done by the same reproductive endocrinologist. Excellent embryologists attend to your reproductive tissue.

Embryo selection for transfer: aiming at transfer of the smallest number of embryos that do the job. Up to age 39 we champion single embryo transfer to minimize twin pregnancy. Sometimes, when appropriate, we employ PGS / PGD to select the best embryo for transfer

#### **IV. Pregnancy Follow up**

10-12 days later you will get a blood pregnancy test, then early pregnancy ultrasounds. The aim is to confirm viability, position and health of the embryo. I then discuss nutrition in early pregnancy. I also explain different options in prenatal screening of chromosomal abnormalities in details. These include quad screen, nuchal translucency, Non Invasive Prenatal Test. Amniocentesis and CVS.

In addition, I describe options on multiple pregnancy and fetal reduction in details. We generally transfer a single blastocyst up to age 39 to the majority of women, minimizing the risk for twins.

*The years of discomfort, time wasted, untoward effects and long waiting should all be behind us. You should be able to get pregnant in few weeks, safely without losing any work*

*time. Fertility treatment can be successful while attending to all other aspects of your life. We want to make sure that you are not dealt a false hope but if there a small hope will go fight for it together till we realize it together.*

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## **Male Factor Infertility: Azospemia**

### **Male Factor Infertility: Azospemia**

Male Factor Infertility: Azospemia means no sperm are found in the ejaculate. Azospemia requires careful evaluation and treatment so that the couple has the best chance to conceive with IVF. The evaluation should be methodical and compassionate to guide the couple through such a multifaceted process to pregnancy and delivery of a healthy child.

### **Four Things Have to Happen at Initial Evaluation for Azospemia**

a. Is it truly azospemia? sometimes repeat sperm analysis together with spinning of the ejaculate multiple times may yield few sperm. This has to be performed by a diligent andrologist and in a facility that can freeze sperm immediately if found. In some azospemic men, repeat analysis and freezing can avoid a surgical procedure to retrieve sperm.

b. A genetic cause for azospemia should be excluded. Specifically three known genetic problems should be excluded because they can be passed to offspring and because they can predict the success of surgical sperm retrieval. A chromosome

analysis should be done to exclude sex chromosome abnormalities e.g klinefelter Syndrome (47XXY). Y chromosome microdeletion study should be conducted to exclude a deletion of the part of Y chromosome related to sperm production. Cystic fibrosis carrier screening should also be run to detect defect in the CF gene that may be associated with absence of the ducts conducting the sperm outside of the testes.

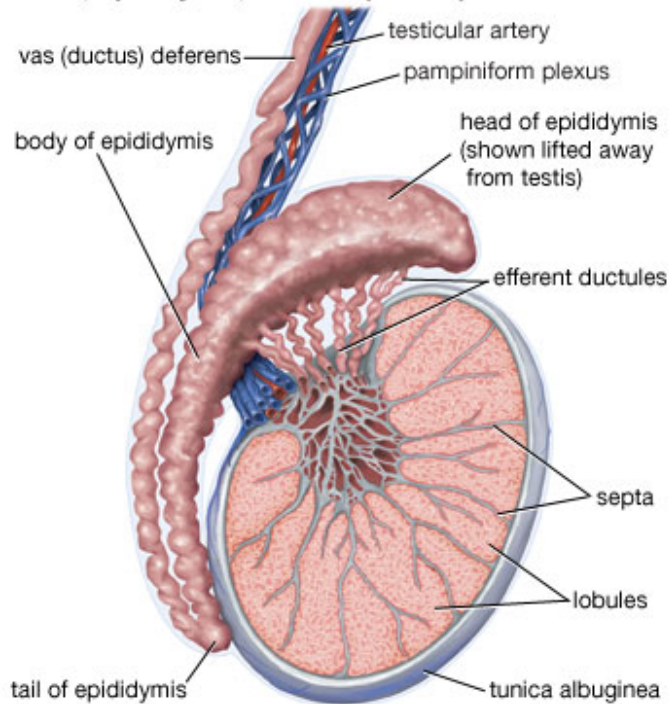
c. Evaluation of Ovarian Reserve for Female Partner. If ovarian reserve evident by day 3 FSH, AMH levels and antral follicle count seen on vaginal ultrasound is not diminished, this predicts reasonable chance for success with IVF-ICSI if sperm are found. Extremely low ovarian reserve or advanced female age may preclude surgical sperm retrieval, unless an donor eggs are acceptable.

d. Urological evaluation. This has to be the last step in evaluation. Male urologists are the physicians specializing in evaluating the chance for successful sperm retrieval (TESE) as well perform these procedures. Before referral by a reproductive endocrinologist and infertility specialist, there should be every reason to think that if sperm were obtained there is a reasonable chance for conception after IVF-ICSI. The urologist should be a specialist in male reproduction and well versed in the techniques of sperm retrieval. You actually need to ask your urologist two questions: what are my personalized chance for finding sperm when surgery (TESE) is performed? What the technique used to obtain sperm? Authorities generally agree that the technique for TESE markedly affect the chance for finding sperm.

Moreover, every workup should end with an important question; would you accept donor sperm if no sperm were obtained after surgery?

## **How is TESE Performed?**

### Testis, epididymis, and vas (ductus) deferens



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### Testes and ducts

Testicular sperm extraction is a surgical procedure that entails sampling of multiple areas of the testes aiming at finding sperm to be used for IVF-ICSI. The testis is delivered outside the scrotum, bisected and multiple biopsies obtained from several areas of the testes. The tissue is examined for the presence of sperm. If no sperm were found, more biopsies are obtained till sperm are found. There are generally two types of azospermia: obstructive azospermia (due to obstruction of the ducts of the testes while sperm production is intact). Sperm is obtained in close to 100% of these cases. Non-obstructive azospermia (NOA) where there is a defect in sperm production, approximately 60 to 70% of the procedures yield sperm.

Blind biopsy from one area of the testes has no place in modern treatment of azospermia. Asking your urologist about the technique of TESE is of paramount importance. The first surgical attempt carries the highest chance for success.

Recently, Doppler ultrasound mapping of the testes can help localize the areas of that should be biopsied because they

yield a higher chance for finding sperm.

## **Why is IVF-ICSI Required after Sperm Retrieval?**

The number of sperm obtained after TESE is small in the magnitude of tens to hundreds of sperm, too small to use the sperm for IUI. ICSI is absolutely required for all cases of surgical retrieval of sperm. The sperm can be used in one of two ways

a. Frozen TESE sperm: The sperm are frozen to be thawed at a later date, on the day of egg retrieval for the female partner. This method saves the cost of IVF if no sperm were retrieved and donor sperm use is unacceptable.

b. Fresh TESE sperm: Ovarian stimulation is started and TESE is performed on the day of egg retrieval or the day before. Fresh sperm are used for ICSI. Donor sperm (if acceptable) is obtained as a backup. Though suggested, there is no concrete evidence that fresh TESE sperm is superior to frozen TESE sperm.

In addition in some cases with associated genetic problems, preimplantation genetic diagnosis (PGD) can be performed followed by the transfer of normal embryos.

## **Can the Chance for Pregnancy be predicted in Male Factor Infertility: Azospermia ?**

There are several predictive factors for pregnancy in female partners of men with azospermia. These can be categorized into:

i. Successful sperm retrieval is related to whether the procedure is the first one or a repeat procedure, the volume of the testes, medical treatment before surgery, the technique used and the cause for azospermia. Some causes are associated

to minimal chance for obtaining sperm.

ii. Pregnancy after sperm retrieval is related to the female partner age and her ovarian reserve. Younger women have a very good chance of conceiving if sperm are obtained. This is the most important factor once sperm are retrieved.

iii. Obstructive azospermia has a higher chance for sperm retrieval than non-obstructive azospermia.

iv. Moving sperm at the time of ICSI has a higher chance to yield a pregnancy than non moving sperm

v. Men with higher testosterone levels and lower LH levels has higher chance of sperm retrieval

vi. The effect of using of frozen TESE sperm is controversial. Some authorities think that using a fresh TESE sperm is better than frozen sperm.

vii. Use of Doppler: recent work indicates that the use of Doppler study of the testes before the procedure may help localize the areas that should be biopsies and yield a higher chance for sperm harvest.

*Male Factor Infertility: Azospermia requires a multidisciplinary approach; first consultation with a reproductive endocrinologist (female age is still the most important factor) followed by a consultation with a reproductive urologist for the TESE procedure for successful sperm harvest and pregnancy*

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# Endometriosis will not Lower IVF Success

## Endometriosis will not Lower IVF Success

Effects of [endometriosis](#) on fertility treatment success has always been a controversy. When a woman is diagnosed with endometriosis, she receives multiple contradicting advises from multiple sources. It is very difficult for women to sort through these recommendations and pick the ***one that are suitable for her symptoms and reproductive plans***. Indeed reproductive plans and symptoms are by far more important than the nature of the problem, anatomically, as well as what one reproductive surgeon or a fertility specialist think you should do.

### Reproductive Plans in women diagnosed with endometriosis

Simply do you want to have a baby or did you complete your family?. If you want to have a baby, then an initial infertility evaluation is required: testing for ovulation, [ovarian reserve](#), male factor and Fallopian tube patency is required. Sometimes other forms of pelvic imaging e.g MRI is needed to test for [ovarian cysts or endometriomas](#)...Endometriosis itself may require laparoscopy and biopsy for accurate diagnosis.

Women are then categorized according to findings: endometriosis only, endometriosis with other factor or endometriosis with low egg reserve. That will facilitate further advice.

*One very important indicator that you are not talking to the right person if he or she did not complete the evaluation for male factor and egg reserve. These are essential tenets of fertility and failure to test them will have impact on success. It would be absurd to do surgery for endometriosis for example to discover later that you have a severe male factor that require IVF -ICSI.*

If you desire future fertility, reproductive endocrinologists should tailor their advice to preserve reproductive tissues and minimize surgery. There is a strong evidence that surgery in the ovary reduces ovarian reserve, irrespective of technique used.

## **Pain in women diagnosed with endometriosis**

If the main symptom is pain, in different forms, then medical or surgical treatment can be employed. in women who completed their families. Medical treatment e.g non cyclic oral contraceptive pills of GnRH agonists (depot lupron) prevent pregnancy. From a practical stand point, surgery in many cases may not promote pregnancy in women with mild and severe endometriosis.

*Women diagnosed with endometriosis and report pelvic pain should focus on getting pregnant. Pregnancy can suppress endometriosis for a long time after delivery*

## **Fertility Treatment in Women Diagnosed with Endometriosis**

**Absolutely avoid doing surgery in the ovaries in women interested in pregnancy.** This is crucial. Opening endometriomas and tripping their walls leads to significant loss of egg reserve. The only indication to remove endometriomas if they are complicated e.g rupture or suspicion



of malignancy. There are many reports of finding eggs in the wall of endometriomas after removal and reduction in egg reserve markers after surgery. Bilateral surgery for endometrioma can lead to menopause, irrespective of the skill of the surgeon.

In minimal and mild endometriosis with reasonable egg reserve, normal sperm analysis and open fallopian tubes, ovarian stimulation and IUI can be entertained in young women (38 years).

In women with moderate or severe endometriosis e.g. endometriomas, blocked tubes.. or those with associated male factor infertility or low egg reserve, IVF yields a much higher pregnancy rate.

## **IVF Success in Women with Endometriosis**

Recent analysis of IVF cycles performed in women with endometriosis with or without other factors (tubal, male, unexplained infertility) indicates that

Isolated endometriosis is associated with similar IVF success and live birth to other infertility factors, though the number of eggs retrieved may be smaller.

Endometriosis when associated with other factors e.g. male or tubal factor may have lower success rates. The live birth rate is still excellent 35 to 45% per cycle.

[Endometriosis-and-IVF](#)

## **Treatment of Endometriosis related pain**

Both medical treatment and surgery are effective for treatment of pain. Endometriomas do not respond to medical treatment. Endometriosis on the peritoneum and other organs respond to medical and surgical treatment. Adenomyosis (endometriosis of

the uterus) is a surgical disease and respond only to surgery.

In general medical treatment is successful but requires patience and can be used for a longer period of time with add back therapy.

*If you are diagnosed with endometriosis there is wide range of treatment options. Treatment should be personalized to your reproductive goals and symptoms not to physician expertise and bias. There is really little controversy about what need to be done in each situation. Women just need to be specific about what they want: get rid of pain or have another baby. IVF success is not impaired in women with endometriosis.*

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## 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 [history, antral follicle count and AMH level.](#)

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.

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# **Anatomy of Ovarian Stimulation Protocol for IVF**

## **Anatomy of Ovarian stimulation Protocol for IVF**

Understanding the anatomy of ovarian stimulation Protocol for IVF or how is the ovary stimulated to produce multiple eggs, helps you understand different medications you are

administering prior to IVF. Understanding the endocrine make up of a woman is essential before selecting and optimizing a protocol including

i. ovarian reserve (and predicting before starting treatment if she is a high, average or low responder)

ii. Age and what is a reasonable response for a pregnancy to ensue

iii. Differentiating between PCOS, hypothalamic amenorrhea and normal ovulatory women.

iv. Other gynecologic problems e.g endometriosis

v. other factors that may lower the response : prior ovarian surgery, medical disorders, chemotherapy exposure ..

vi. What are the specific aims of IVF in addition to pregnancy e.g PGD..

After evaluating these factors for each woman, different options are selected for stimulation prior to IVF. There is no place for one protocol fits all. Its a diligent thinking of what works best, one patient at a time.

## **Adjuvants**

These are medications given prior to menses or during the cycle to improve response to gonadotropins

Estradiol: oral or vaginal to synchronize the follicles, so that they are equal before starting stimulation so that they end the cycle close to each other at the time of egg retrieval

Antagonist: to prevent a premature growth of follicles prior to starting stimulation so that we obtain a synchronized group of follicle.

Oral contraceptive pills: we do not use birth control for timing of the cycle most of the time but sometimes to obtain a

regular group of follicles before starting stimulation

Testosterone: testosterone gel for 2-3 weeks has been shown in randomized clinical trials likely because of sensitizing the ovary to the effects of stimulation medication. No other androgen preparation has been demonstrated to improve pregnancy outcome including DHEA.

Clomid or letrozole: these oral medications may improve response through release of internal FSH from the master gland.

Other medications suggested to improve response with weak evidence that they actually improve the pregnancy rates e.g Growth Hormone

## **Prevention of premature ovulation**

One landmark improvement in stimulation protocols is the addition of medicine that prevents the master gland in the brain from triggering ovulation prematurely. Two options are available agonist or antagonist

Agonist in a short protocol (flare lupron) or long protocol

Antagonist starts during the cycle when the largest follicle reach 14mm and estradiol level 300pg/mL

Each have its advantages and merits and they are generally used for women with different endocrine environment. Antagonist protocols gained more dominance in the past decade.

## **Gonadotropins**

Two main types of gonadotropins exist in the US; Pure FSH and a mixed FSH + LH preparation. FSH is the main stimulating medicine but in some women the addition of LH improves the response. Many women receive mixed FSH and LH protocols.

The dose of such medicine starts at the highest dose then is drops gradually, the step down protocol. The initial dose

depends on egg reserve, weight and expected response. Usually the maximum starting dose is a total of 450 units.

*Some reproductive endocrinologists recommend Minimal stimulation IVF* in select patients. There is no proof that the concept one healthy egg is correct. As a matter of fact many women produce many healthy eggs in the same cycle. There is no evidence that cycle for cycle they produce comparable pregnancy rate. Proponents of multiple stimulation recommend multiple cycles to produce multiple embryos.

## **Ovulation Trigger**

When your reproductive endocrinologist perceive that the eggs are close to maturity, she or he employs a triggering agent to finalize follicle maturity and prepare the eggs for retrieval. Two agents are available

hCG given in muscle or under the skin. Its associated with higher incidence of ovarian hyperstimulation.

Agonist (Lupron) trigger given under the skin and has a short duration of action. It prevents ovarian hyperstimulation syndrome.

## **The Length of Stimulation**

In general, shorter the stimulation the better the outcome. The earlier the the trigger shot is administered the better the quality of the eggs. Longer stimulation increases the exposure of eggs to gonadotropins and likely lower the quality of eggs.

## **Luteal phase Support**

Every woman stimulated for IVF require luteal phase support as progesterone production after retrieval is defective. Two preparations exist

Progesterone in the muscle. This is the classic way of

supplementing progesterone. Its very stable but require injections and also can cause allergy.

Vaginal progesterone. Recently introduced, used twice a day using an applicator in the vagina.

*Many aspects of stimulation protocol need to be considered in each patient to ensure optimal stimulation of the ovaries, best possible egg yield and subsequently the highest number of good quality embryos and highest pregnancy rate. Sometimes changing the protocol is better for women than to continue with a protocol that is less productive and associated with low pregnancy rate. The talent, care and experience of reproductive endocrinologist is central to selection appropriate stimulation regimen*

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## **Medically + Economically You Should Avoid IUI at Age 38**

### **Medically + Economically You Should Avoid IUI at Age 38**

Medically and Economically you should void IUI at age 38 or older. Couples facing difficulty conceiving and after completing a fertility workup, they have three general fertility treatment options. Regular intercourse, ovarian stimulation with oral medications ([clomid](#) or [letrozole](#)) or [injection medications](#) followed by IUI (COH-IUI) or [IVF](#).

The chance for pregnancy is very low with COH-IUI that you may as well just try with intercourse. The likely cause is



production of a small number of eggs with these stimulation protocols, lowering the chance of encountering a chromosomally normal eggs. IUI in itself slightly increases the pregnancy rate but the main benefit in fertility treatment is produced through ovarian stimulation and recruitment of multiple eggs.

On the other hand, IVF carries a very good chance for getting pregnant. If not ready for fertility treatment just have regular intercourse. If ready, proceed directly to IVF as you will realize much higher success rate and save also on treatment with minimal yield (IUI). Here is a synopsis of published studies ([asrm.org](http://asrm.org)).

## **Traditional egg reserve tests**

Women who initiated infertility treatment with FSH of 10 to 15 mIU/mL and E >40 pg/mL on day 3 testing were unlikely to achieve live birth after COH-IUI treatment. In two well designed studies on 603 patients contributing 2,717 total cycles, no live births occurred during COH-IUI. IVF still afforded these patients a reasonable chance of success (6/18 couples, 6/40 cycles, 33.3% live-birth rate per couple).

## **Female Age**

*Age ≥ 38 to 42y:*

*The cumulative clinical pregnancy rates per couple after the first two cycles of CC/IUI, FSH/IUI, or immediate IVF were 21.6%, 17.3%, and 49.0%, respectively. After all treatments, 110 (71.4%) of 154 couples had conceived a clinically recognized pregnancy, and 46.1% had delivered at least one live-born baby; 84.2% of all live-born infants resulting from treatment were achieved via IVF. There were 36% fewer treatment cycles in the IVF arm compared with either COH/IUI arm. Also couples conceived a pregnancy leading to a live birth after fewer treatment cycles.*

Age 21-39:

Per cycle pregnancy rates for CC/IUI, FSH/IUI, and IVF were **7.6%, 9.8%, and 30.7%**, respectively. Average charges per delivery were \$9,800 lower (\$25,100 lower to \$3,900 higher) in the accelerated arm (IVF) compared to conventional treatment (IUI).

## **Other Fertility and Social Factors to consider**

There are other factors to consider: moderate to severe male factor and blocked tubes makes IUI and intercourse not an option. Absolute cost and insurance coverage are maybe important (although its by far more cost effective). Risk of multiple pregnancy should always be considered especially with Injection +IUI cycles. Some couples have personal "resistance" to adopting IVF as difficult, uncomfortable, risky or unnatural, and that autonomy has to be both respected and embraced but also discussed. Their sentiment has to be balanced against a 7% per cycle pregnancy rate if you do Clomid-IUI, 9% per cycle injection -IUI (both become zero if egg reserve tests are abnormal) *versus* 35%pregnancy rate with IVF.

Knowing the expected rate of success is an integral part of fertility counseling.

## **Medically + Economically you should avoid IUI at age 38**

*All being equal, for modern couples, the most humane approach is to get them pregnant before the short favorable window of reasonable number and quality of eggs wane. No to do so means letting them enter the into the more difficult phase of final reproductive years. Treatment success drops in late reproductive years to a single digit and they jeopardize their chance of having a baby.*

[FORTT](#)

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# Fertility Apps Do not Help You Get pregnant

## **Fertility Apps Do not Help You Get pregnant**

### **Beyond Regular Intercourse**

Many women use fertility apps to track their menstrual cycle and time intercourse. Tracking cycles, using apps as method of registering when the cycle started and ended is fine. The use of apps to time intercourse is not supported by any scientific evidence. We know for a long time that conception is likely to occur when exposure to sperm takes place in the six days that end in ovulation.

### **Why Fertility Apps are Unlikely to be Helpful**

An analysis of large number of apps and websites indicates that only a minority will yield that fertile window and thus are unlikely to help women get pregnant.

Variation in the length of menstrual cycle 21 to 35 days will also means that ovulation day is very difficult to predict with methods readily available for women. Early ovulation (day 6 or 7 of the cycle) as well as late ovulation (day 18 to 20) will be missed. Conception will be a possibility in these cases for women having regular intercourse.

Sperm survives for at least 3 days. The WHO in a large study indicates that intercourse 3 times a day yields highest pregnancy rate among normal couples. Conceptually if you have

intercourse 3 times a day, after menses, you have exposure to sperm all the time and there is no need to time ovulation. More accurate timing of ovulation using many self administered methods has so far to demonstrate increase in pregnancy rate. More recently survey of more technology mediated methods also failed to show an increase in pregnancy rate beyond regular intercourse.

## **Effectiveness of Fertility Apps**

Beware of many writings about [fertility apps](#), what do they do and what do they do not do..They miss the most important piece of information. Do they enable you to get pregnant at higher odds than those not using the app? And of course they cannot accurately answer that question as they did not do the research that prove an improvement in pregnancy rate. Many articles about fertility apps start with the narrative assumption that they are effective without offering a reference or proof.

One recent scientific survey of over 50 apps indicated that most of them even miss the fertile period. Insisting on intercourse at a specific day is not helpful also can impair performance in men.

## **How Long Have you Been Trying to Conceive (TTC)**

It's exactly how long have you been having intercourse not protected by a birth control (pills, condom), irrespective of use of apps or any other method of timing ovulation. Not accounting for this period, artificially shorten the duration of infertility and delay seeking medical care.

It's great to use technology when it helps, it gives women a sense of empowerment. But when technology is not proven to be helpful then simple proven solutions should be used.

## **Possible Harm Caused by Using Apps**

When you use fertility apps alone to conceive you are in

effect

1. Depriving yourself of other fertility tests. You will not know if your partner sperm is normal or if your Fallopian tubes are open. Your egg reserve is also not evaluated. All these factors are important for decision making about fertility and how long you should continue to try using the app. For example, if your tubes are blocked or your husband sperm is low intercourse close to your ovulation will not be helpful leading to more time wasted and no improvement in chance of conception.

2. Preconception testing and counseling performed at initial fertility evaluation is skipped. That means the risk of common genetic and other diseases are not tested for e.g cystic fibrosis, sickle cell disease, spinal muscular atrophy, Ashkenazi Jewish Profile and others. These increase the risk of transmission of genetic diseases to the baby. Other infectious diseases are not tested for too e,g hepatitis, immunity to Rubella and chicken pox.

3. [Serious security and privacy flaws has been cited for some fertility apps](#). Fertility apps ask users for intimate details including weight, sex life, pregnancy, miscarriage.. [A recent consumer report](#) indicated that someone with no hacking skills can access all these data. Data are also shared without permission with other apps

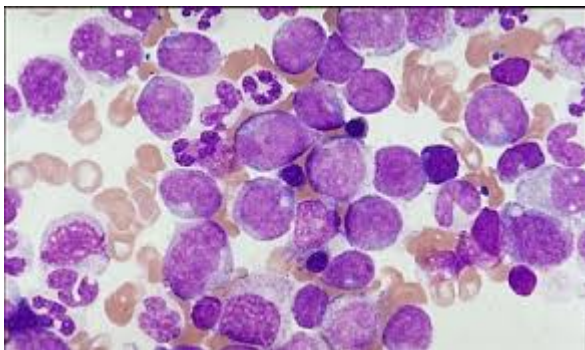
**Do not use apps and have regular intercourse 3 times a week. Fertility Apps Do not Help You Get pregnant beyond Regular Intercourse and Delay a Complete Fertility Testing.**

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# Fertility in Women Diagnosed with Chronic Myeloid Leukemia

## Fertility in Women Diagnosed with Chronic Myeloid Leukemia

Women and men diagnosed with chronic myeloid leukemia should consider fertility issues and safety of pregnancy while under treatment. Chronic myeloid leukemia (CML) is formed of malignant cells from the bone marrow. It may later spread to the blood stream or other organs. It may also progress to a fast growing stage-acute leukemia. It is diagnosed in 2000 women and 2800 men yearly in The US, mostly during their adult years. Most individuals diagnosed with CML carry an abnormal chromosomal arrangement called Philadelphia chromosome. Many patients do not have any symptoms. CML is suspected from blood



counts and confirmed by examining blood smears and bone marrow examination.

Newer drugs like imatinib, dasatinib and nilotinib have changed the treatment of CML dramatically. More than 90% of patients that received these medications survived for 5 years or more. These belong to a group of medications called tyrosine kinase inhibitors (TKIs). These medication slow the propagation of lymphoma cells. Their side effects are less than standard chemotherapy. Response to treatment is assessed using blood counts, the presence of Philadelphia chromosome and molecular genetics tests for a specific gene. Some individuals require stem cell transplantation. Transplantation requires treatment with high dose chemotherapy and total body

irradiation, both are associated with very high risk for ovarian failure.

**Effects of TKIs on fertility.** *Animal studies* indicate that exposure to TKIs during adult life was not associated with impaired fertility in males and females. Exposure before puberty lead to reduced sperm production in males. There has been few case reports of low sperm count and early ovarian failure after exposure to imatinib in *humans*. This was not reported in large studies. Because of the possible effects of imatinib on fertility and because all individuals treated for CML are at risk for progressive disease requiring stem cell transplantation, men and women diagnosed with CML should consider fertility preservation. Men should consider sperm freezing. Women should consider embryo cryopreservation (if they have a partner) or egg freezing.

**Effects of leukemia on pregnancy.** In general pregnancy itself does not appear to affect the prognosis for leukemia There is no evidence that brief exposure to imatinib in early pregnancy is associated with adverse outcomes or abnormalities in the babies. There are no extensive data, however on the effects of imatinib and data on the effects of newer TKIs dasatinib and nilotinib are very sparse. Women are usually advised to use a birth control method while on these medications. In one study two of 16 babies had minor abnormalities (hypospadias in one baby and rotation of small intestine in one baby) that were surgically repaired. Women who were in remission and chose to stop imatinib during pregnancy, had 40 to 50% chance of showing evidence of propagation of the leukemia cells. The majority of them though achieved remission again after re-starting treatment.

Children born to men who are actively taking imatinib at the time of conception appear healthy and current advice is not to discontinue treatment. This is based on outcomes of 60 pregnancies reported worldwide in female partners of imatinib-treated men. In contrast the data relating to

children born to women exposed to imatinib during pregnancy are less encouraging. Although numbers are small-12 congenital anomalies were found among 125 pregnancies-there has been a cluster of rare congenital malformations such that imatinib cannot be safely recommended, particularly during the period of organ formation in the baby-first 8 to 12 weeks.

Women interested in getting pregnant while on imatinib and other TKIs should co-ordinate their specific care between oncologists and reproductive endocrinologist so that they attempt pregnancy while in remission for ideally 1-2 years and in the same time minimize the period of time while off treatment. Alternative treatments than TKIs can be used during pregnancy. After delivery, TKIs are restarted and breast-feeding is discouraged as the medicine is excreted in milk. Read more at <http://nycivf.org>