

# 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](#)).

## **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.*

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## **What if You Have Dual Infertility Factor**

### **What if You Have Dual Infertility Factor**

Many Times You Do

Infertility factors are generally classified into [tubal factor \(blocked fallopian tubes\)](#), [male factor \(abnormal sperm concentration, movement or shape\)](#) and [ovarian factor \(no ovulation\)](#). In the majority of situations though multiple factors exist. If you partner has low sperm count, you also may have a blocked tube. Women who do not ovulate can also have endometriosis. Some men think that their female partners are infertile due to a female factor while they also have subtle sperm abnormality that prevents fertilization. Women sometimes think their male partners sperm is abnormal while

they also have low egg reserve and low egg quality. *Couples potentially have a dual infertility factor, most of the time.* Most notably, low egg number and quality should be considered in any couple seeking fertility evaluation and treatment. Even young women with good egg reserve have abnormal eggs.

Irrespective of infertility factors, consideration of other general factors e.g genetic screening results can have a significant impact on choice of fertility treatment modality. If both partners are carriers for cystic fibrosis, they may require embryo testing (PGD) in the setting of IVF as opposed to similar couples without this genetic risk factor.

## **Do not Accept Treatment Before a Complete Workup. Do not Accept Empiric Treatments**

For that reason, no assumptions about fertility factors and treatment should be made before a completed workup for sperm, ovulation, ovarian reserve, Fallopian tubes and general factors (genetic and preconception screening). This careful and deliberate testing is unfortunately not always followed. In many cases, couples are treated with empiric treatments. Here are two very common empiric treatments commonly prescribed

a. [Clomid used for everyone](#). Clomiphene is suitable as initial treatment for women who do not ovulate due to polycystic ovary syndrome (PCOS), have open tubes and normal sperm analysis. In modern reproductive medicine, clomid should not be used without testing of male and tubal factor. Clomid also should not be used in older women that ovulate regularly. The majority of these women are older and do not get pregnant because of lower egg quality. They require superovulation (more than one eggs) to compensate for lower egg quality.

b. Progesterone supplementation. Low progesterone can cause early miscarriage (not infertility) in a small percentage of women. Women that yield low progesterone after ovulation do so

because of abnormal development of follicles. They are better served by induction of ovulation to produce better follicles, rather than progesterone supplementation. During fertility treatment, progesterone levels are monitored and maybe supplemented if low. Progesterone treatment in itself is not a treatment for any form of infertility.

c. [Laparoscopic surgery for endometriosis](#). The magnitude of benefit for surgical treatment of infertility associated with endometriosis is limited and maybe harmful. Laparoscopic surgery for severe endometriosis is risky e.g bowel injury. Resection of endometrioma can reduce ovarian reserve. IVF is a better than laparoscopic surgery in treating infertility due to moderate and severe endometriosis . The increase in pregnancy rate after excision of mild endometriosis is limited (probably 30 surgeries are needed to produce one newborn).

d. [Varicocele repair for male factor infertility](#). Although sperm parameters may improve after varicocele repair, there is no conclusive evidence that it will translate into higher odds of pregnancy in female partners. There is a limited indication for varicocele repair aiming at improving fertility in males.

Many of these empiric treatments and prescribed with no or limited scientific basis and represent bias and expertise of the prescriber.

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**Endometriosis: Fertility Options are Clear**

# Endometriosis: Fertility Options are Clear

Endometriosis means tissue of the lining of the uterus is present outside its normal boundaries. It can involve the pelvic lining, the ovaries (endometrioma), the fallopian tubes, the intestine and the muscle of the uterus (adenomyosis). As menstruation takes place in the uterus, these deposits menstruate into itself, become distended and causes pain (pain with menstruation, chronic pelvic pain, pain with intercourse, urination or defecation). Moreover, because of its chemical effects or associated pelvic scarring endometriosis may cause infertility.

Accurate diagnosis of endometriosis requires laparoscopy and biopsy of the areas suspicious because of its appearance. If you are suspect you have endometriosis (usually because of pelvic pain) and want to get pregnant or having difficulty becoming pregnant you face a small dilemma. You are usually given different recommendations from different headquarters, depending on their expertise and biases. Examples of such recommendations:

'Lets do laparoscopy to diagnose endometriosis, remove any endometriosis we find as well as remove any scarring'

'Lets give you medications for endometriosis'

The question is which recommendation is "good for your specific case".

## **Few basic principals about endometriosis treatment**

These are not disputed principals, just facts related to the treatment of endometriosis in general.

1. Accurate diagnosis of endometriosis requires a laparoscopy and pathological examination of tissue biopsies obtained.

2. Medical treatment of endometriosis does not allow you to get pregnant while you are using it: oral contraceptive pills, synthetic progesteron, danazol and GnRH agonists (lupron) prevent ovulation. While you are taking these medications you will mostly not ovulate so you will not get pregnant.

3. Endometriomas (endometriotic cysts of the ovary) do not respond to medical treatment. Moreover their removal mostly require removal of a part of the ovary, because they are firmly attached. Thus their removal can lower the number of eggs remaining in the ovaries (ovarian reserve).

## **Treatment of infertility associated with endometriosis**

Though each specific situation may require a different course of action as recommended by your physician, there are general guiding principals for treatment of infertility when endometriosis is suspected.

1. **Infertility investigation:** do not make any treatment decisions without a full fertility workup. Do not proceed unless you know your partner [sperm analysis](#), obtained the results of [ovarian reserve tests](#), tested if your fallopian tubes are open or not via an HSG as well as general [preconception lab tests](#). Why? if you undergo surgical treatment for endometriosis and later discovered that your partner has very low sperm count requiring IVF and ICSI, then surgery had no potential to help you get pregnant.

2. **What is your priority treating infertility or treating pain?** This is important because medical treatment, although effective in treating pain cannot help you with infertility because it mostly prevents ovulation. Please note that the best treatment for pain associated with infertility is pregnancy. The large amounts of progesterone produced during pregnancy suppresses endometriosis, sometimes for years after delivery.

3. **Resection of endometrioma**; If a cyst consistent with endometriosis is seen on ultrasound be very careful with a recommendation to resect that cyst. Resection requires surgery. it reduces ovarian reserve because of removal of ovarian tissue. Unless the cyst is suspicious of malignancy or complication they are better left alone with observation while proceeding directly to fertility treatment e.g IVF. There is no evidence that removal of the cyst improves IVF success. On the contrary, removal of the cyst is associated with low response in that ovary.

4. **Laparoscopic surgery for mild and minimal endometriosis**: There are two studies that showed an improvement in pregnancy rate after laparoscopy for mild endometriosis. To put this in perspective, yes laparoscopy for infertility and mild endometriosis and infertility is an option but the magnitude of benefit in this case is limited at best. You first have to undergo surgery (with its possible complications). If endometriosis is found and ablated you would get a small bump in pregnancy rate in the year following surgery. The surgery may also help you with pain. On the contrary, endometriosis may not be found and you still have to try after surgery. Considering all the risks and benefits, the odds for pregnancy is not dramatically improved.

5. **An alternative approach to mild and minimal endometriosis**: The general thinking about infertility associated with minimal and mild endometriosis is that it is unexplained infertility. In these cases there is no mechanical distortion of pelvic organs and fallopian tubes are open. If sperm analysis is within normal enhancing fertility could be achieved through stimulation of the ovary to produce multiple eggs followed by IUI or IVF. This approach avoids surgery with its potential complication. IVF carries approximately three times the odds of pregnancy and can control the risk for multiple pregnancy, compared to IUI.

6. **Moderate to severe endometriosis**: These cause distortion or

blocking of the fallopian tubes. Surgery is an option but its much more complicated than mild cases and has the risk of injury to the intestine, ureter, fallopian tubes, ovaries..Scarring also may recur after surgery. An alternative approach is to proceed to IVF. It avoids major surgery and can address tubal, male and ovulatory factors. IVF success is not reduced in women with endometriosis.

7. **Adenomyosis (endometriosis of the uterus)**: MRI is sometimes needed for accurate diagnosis of adenomyosis. Adenomyosis is a surgical disease and its cure require removal of the whole uterus. This is because it cannot be shelled out of the uterus like a fibroid. Better ignored and proceed with fertility treatment.

Do not make any decisions related to infertility before a complete workup; sperm analysis, ovarian reserve tests and fallopian tube patency test. Avoid surgery in the ovary as it may reduce ovarian reserve. There is no established evidence that the chance for successful fertility treatment is reduced in women with endometriosis. Laparoscopic surgery is an option but is associated with surgical complications.

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## **Even with Diminished Ovarian Reserve You Can Achieve Pregnancy**

**Even with Diminished Ovarian Reserve You**

# Can Achieve Pregnancy

## Diminished Ovarian Reserve: What Does it Means

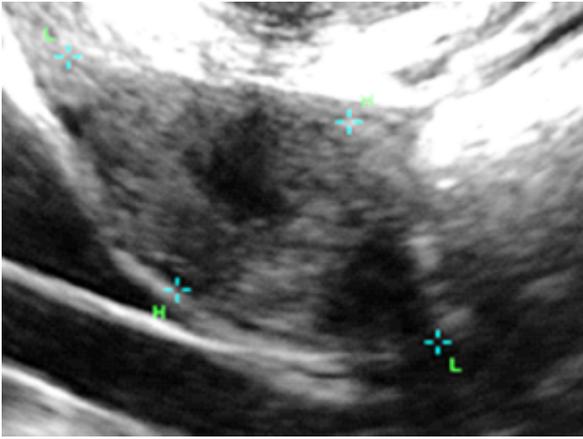
The number of eggs and their quality are reduced at a given age. Women with diminished ovarian reserve have less eggs and more chromosomally abnormal eggs than women in the same age group. It reflects low response to fertility medications and more difficulty achieving a pregnancy. Women with diminished ovarian reserve may reach menopause one or more years earlier. As few eggs remain, still some of the eggs are chromosomally normal and pregnancy is very possible in women with diminished reserve.

## Diminished Ovarian Reserve: How it is Diagnosed

**History:** Some historical factors may indicate low reserve including cigarette smoking, prior surgery of the ovary (removal of a cyst or an ovary), prior exposure to chemotherapy (particularly cyclophosphamide) or pelvic irradiation, early menopause in other family members (mother, sister), recurrent early first trimester pregnancy loss (indicating low egg quality) and others.

**Day 3 FSH:** It is an indirect marker for ovarian reserve. It is produced by the master gland in the brain. levels > 12mIU/mL indicates low reserve. It is less accurate than AMH or ultrasound.

**AMH:** is a protein produced by the cells surrounding the egg in small size follicles. It is more accurate than day 3 FSH. Levels <1.5ng/mL indicates low reserve



Low antral follicle count  
(Ovarian Reserve)



Good antral follicle  
count (Ovarian  
Reserve)

**Vaginal Ultrasound:** in expert hands (a reproductive endocrinologist), it is an accurate measure for ovarian reserve. The number of small follicles  $<10\text{mm}$  especially on day 2-5 of menstrual cycle is an accurate indicator for ovarian reserve and response to fertility medication. The presence of an advanced follicle  $>13\text{mm}$  on day 2 or 3 is also an indicator for low reserve as it indicates that the ovary is under increased stimulation from FSH produced the master gland.

More details on ovarian reserve tests can be found [here](#).

### **Diminished Ovarian Reserve: What Should you Do**

If all other fertility factors (male factor, tubal factor..) are normal *you should attempt to conceive irrespective of*

*ovarian reserve*. Ovarian reserve tests are not absolutely accurate. They do predict response to ovarian stimulation but are not very good in predicting pregnancy. Two general options exist: i. regular intercourse or ii. ovarian stimulation to produce more than one egg followed by IUI or IVF.

## **Diminished Ovarian Reserve: What Should your Reproductive Endocrinologist Do**

Your reproductive endocrinologist should ascertain ovarian reserve with multiple modalities: ultrasound and blood work. The infertility workup should be completed first: sperm analysis, hysterosalpingogram test for patency of fallopian tubes as well as preconception labs. Your infertility specialist should be able to advise you on the treatment protocol that is more likely to achieve a pregnancy. *Fertility specialist should not deny treatment to women based on diminished ovarian reserve*. Every woman with diminished reserve should be offered treatment at least once.

If the treatment plan involves ovarian stimulation, a special stimulation protocol or adjuvant treatment should be considered hopping at increasing the ovarian response (number eggs produced during the cycle). Some of the modifications commonly used are increasing the dose of gonadotropins, use of antagonist or flare antagonist, addition of clomid or letrozole, pretreatment with testosterone and use of growth hormone.

## **Diminished Ovarian Reserve: What would you expect from fertility treatment**

Well it depends on few factors: **Age and Relative Response to Fertility Medications**

If a younger women e.g <37 years produce two or three good quality embryos at the end of stimulation, they have a reasonable potential to achieve a pregnancy after IVF. The chance of getting pregnant in women older than 40 with few

embryos is much lower. When one compare effects of low ovarian reserve and age on reproduction it is clear that age has more negative effect on reproduction than age. Age is associated with low egg quality while ovarian reserve mainly speak for the number of eggs in the ovary. *Younger women with low egg production fairs much better than older women with good reserve.*

Response to ovarian stimulation is not created equal. Women that produce four or more large follicles >15mm are at much better chance for pregnancy after IVF. On the other hand those that have lesser response <3 follicles are a much lower chance for success and should consider converting their cycle to IUI or just cancel the cycle if they have male or tubal factors. They then can try again after considering a modification of the stimulation protocol. In women that produce > 3 -4 eggs IVF is substantially more successful (about three times) than IUI.

Because the response to fertility medication is difficult to judge just based on ovarian reserve markers, most women should be encouraged to try ovarian stimulation once at least and most women should not be denied treatment based on the notion of low ovarian reserve.

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## [Fertility Treatment for Busy Professionals](#)

### **Fertility Treatment for Busy**

# Professionals

## From TTC to a Viable Pregnancy

If you and your partner has been trying to conceive (TTC) and your busy with work commitments, here are few tips that help you save time and shorten the time to conceive. Understanding few basic fertility concepts are helpful. What is fertility? It is the ability to conceive with regular unprotected intercourse. If you are having adequate frequency of intercourse, *then you have been trying, irrespective of timing of intercourse.* If this goes on for one year, if less than 35 or 6 months if 35 or more, then you are having difficulty getting pregnant. Female age is the most important fertility factor

Percent of currently married, childless women 15-44 years of age who have impaired fecundity by current age (from [CDC: The National Survey for Family Growth](#)):

	<b>2002</b>	<b>2006-2010</b>
<b>Total 15-44 years</b>	25.3%	21.2%
<b>15-29 years</b>	17.3%	11.0%
<b>30-34 years</b>	24.5%	14.2%
<b>35-39 years</b>	33.9%	39.3%
<b>40-44 years</b>	42.8%	47.1%

The longer you try, without conceiving, the stronger the indication that you have a significant problem with fertility.

The factors that need to be tested at initial workup include:

- i. Ovulation and ovarian reserve
- ii. Fallopian tubes: open or not
- iii. Male factor: sperm analysis and

iv. General factors related to safety: infectious diseases and genetic carrier screening.

But how do you get all that done, understand the results, decide with your reproductive endocrinologist on a **fertility treatment** plan and execute the plan promptly, while you handle your daily work and life engagements? A coordinated effort between you, your fertility specialist and other personnel enables you to promptly understand your fertility potential. A flexible reproductive endocrinologist can grant you an appointment at a time that does not disturb your work schedule. At your initial visit, ultrasound is performed for evaluation of ovarian reserve and any abnormalities in the uterus. In the same day, blood is drawn from you and your partner and can be sent for testing. Also a sperm sample can be submitted in the same day or few days later for sperm analysis. Hysterosalpingogram (HSG) can be performed by your physician or a radiologist within 1-2 weeks. Then, Can you communicate electronically with your physicians? This enables efficient discussion of lab results and subsequent steps.

How Fast Can You Decide on a [Fertility Treatment](#) Plan? It depends on many factors related to the complexity of fertility issues uncovered during the workup, need for surgery e.g. to remove fibroids, polyps or dilated fallopian tubes, proposed fertility treatment, need for genetic testing of embryos (PGD) and need for third party reproduction (donor eggs, donor sperm, gestational carrier). If complex treatment is required usually a second visit is helpful for evaluation of the uterine cavity, trial transfer, training on fertility medication self administration. Handling of insurance and dispensing fertility pharmacies also help reduce the burden on women busy with work engagements.

Many women are advised to continue to try to conceive naturally (3 to 6 months). For those requiring fertility treatment usually a fertility treatment plan can be executed in 10 to 20 days and within 5 to 8 visits. Again the

flexibility of the practice in scheduling and communication allow you to execute around your daily work and family commitment.

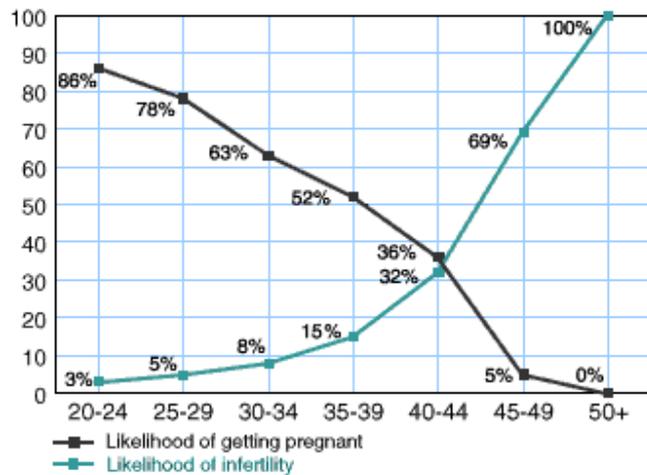
The flexibility of the fertility clinic, efficient planning of visits and use of secure electronic communication methods enables women to go through fertility treatment with minimal inconvenience and work interruption.

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## [Fertility Options for Single 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, [egg freezing](#) 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.

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# Fertility Treatment: Do not be Distracted



Fertility Treatment: do not be distracted by worthless recommendation

## **Fertility Treatment: Do not be Distracted**

When contemplating options for fertility treatment with your own eggs, it always boils down to continue frequent intercourse, ovarian stimulation / ovulation induction + IUI

or some form of IVF. During consultation or when weighing your options do not lose perspective of the big picture. Many suggestions may present themselves and serve to distract you. Men and Women load up on these distractions from the web, friends, primary care physicians or the couple themselves. Some of these recommendations are harmful because they shift the focus to non-proven interventions and most notably cause delay consultations with a reproductive endocrinologist and completing the infertility workup or starting treatment if needed.

## **Do not be distracted by these arguments**

### **I am *Healthy***

Many women in America consider being healthy as being fertile. The media also bombard us with photos of beautiful women in their forties with babies. Truly many women, are in great shape with ideal body weight, exercise regularly, have no medical problems and feel great about themselves.

Fertility though speaks to a specific set of factors related to the ovaries, fallopian tubes and quality of sperm. Healthy women can have low egg reserve or blocked fallopian tubes or their partners have low sperm counts. Hence their fertility could be impaired. On the other hand, women not leading a healthy lifestyle or having a medical disorder can be very fertile if all fertility factors (tube, ovary, sperm) are functional.

### **I did not try enough**

If you do not use birth control pills or condoms and you have having regular intercourse, then you are trying, irrespective of your conscious intentions. If you are you had regular intercourse for one year and are younger than 35 years or six months and 35 or older, then you have tried. Regular intercourse means two to three times a week. If you had

intercourse with reasonable frequency for 6 months to a year and you are not pregnant consult with a fertility specialist. There is a strong relationship between the length of trying and pregnancy rate. The longer that you have been trying, the lower the chance for spontaneous conception.

## **I did not time my ovulation**

Timing your ovulation is not required at all if you are trying to conceive. Actually timing your ovulation maybe harmful to your chance to conceive. Because the methods you would use to time ovulation (cervical mucus, ovulation prediction kits, basal body temperature or intelligent thermometers and apps) are not accurate, you may miss valuable time and have intercourse at the wrong time if ovulation takes place unexpectedly early. Moreover, you cannot get higher odds for getting pregnant above and beyond having intercourse three times a week because sperm will be available all the time when you ovulate. Several studies failed to show any increase in pregnancy rates using many of these timing methods.

## **On Fertility Apps and other monitors**

Many (>4 million) websites discuss times intercourse utilizing other methods (fertility monitor, cervical mucus, calendar methods, urine LH kits..). More recently [technology entrepreneurs](#) are delved into the “trying to conceive” area and volunteered advice. There is no evidence to support that any calculation method improves the odds of getting pregnant over frequent intercourse. These non-scientific advice is a major distraction. Even if these apps collected data on how many women got pregnant, without a comparison group, is not a prove that they actually work. [One study indicated that timed intercourse is associated with higher incidence of erectile dysfunction \(43%\) and extramarital sex \(11%\).](#)

## **My progesterone level is not optimal**

For almost all women, low progesterone level is not a cause for infertility. In natural cycles, progesterone starts to rise after ovulation. Levels of 3 nanogram/mL or more indicates ovulation, Optimal levels to maintain the lining of the uterus are 8 to 10ng/mL. Levels less than 8 (luteal phase defect) may lead to miscarriage because progesterone is not adequate to maintain the lining of the uterus but it is not a cause for not getting pregnant (infertility). Progesterone is monitored, and supplemented if low, during fertility treatment but in itself low progesterone is not a cause for infertility.

## **On Clomid & Letrozole**

Clomiphene is widely used as initial fertility treatment. This use is commonly not appropriate because

- a. clomid is used without infertility workup (checking ovarian reserve, sperm analysis and fallopian tubes)
- b. clomid is used without performing basic tests related to the safety of getting pregnant (infectious disease and genetic screening)
- c. clomid is used by women that are not likely to benefit from it e.g regularly ovulating women with low ovarian reserve and unexplained infertility. Women that are most likely to benefit from clomid are women with chronic anovulation e.g women with polycystic ovary syndrome (PCOS).
- d. clomid is commonly used with no monitoring using ultrasound. If you do not get pregnant, one would not know if you did ovulate or not. 10-20% of women do not respond to clomid. If you are destined to get pregnant, there is a possibility that you have many eggs developing in the ovary because you are unduly sensitive to the medicine. Strong response to clomid makes you at risk for multiple pregnancy

e. clomid is commonly use for extended periods of time while the majority of pregnancies take place in the first 3 months.

f. IUI is preferred to intercourse only, in clomid cycles because it can cause the cervical mucus to be thick. IUI bypasses the cervical mucus and deposit the sperm into the cavity of the uterus

g. Letrozole is similar to clomid regarding the use and indication but there is evidence that pregnancy is higher after letrozole compared to clomid.

Use clomid or better ltrozole for the right indication, with monitoring and for 3 (max 6) months only.

## **On Setting Time Limits**

For each fertility treatment step: intercourse, ovarian stimulation + IUI or IVF define the number of cycles you will try before proceeding to the next step. Statistically, these treatments are more likely to succeed in the first three treatment attempts. Subsequently, the chance for getting pregnant diminishes and you and your physician should consider moving to another treatment.

## **Do not loose track of your age and ovarian reserve**

You have normal fallopian tubes and partner sperm and you ovulate every month. Younger women are encouraged to try (have regular intercourse). The duration of trying on your own should be guided by ovarian reserve tests and age. Younger women with good reserve can try a bit longer than older women or women with low reserve. This recommendation should be based on scientific information not general perception. *Do not accept the advice 'keep trying' from any one without considering you age and without performing the tests for ovarian reserve (vaginal ultrasound, AMH and FSH on day 3).*

*Female age is the most important factor in occurrence of a healthy pregnancy and should be the prime consideration even if ovarian reserve tests and other factors are normal.*

There is a plethora of low quality information, recommendation and advice out there. Women accumulate them from multiple sources or just using their simple logic. They can lead to delay in fertility testing and fertility treatment that could be detrimental to future fertility.

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## [Fertility Treatment Options](#)

### **Fertility Treatment Options: What Are Infertility Treatments?**

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Following detailed fertility investigation of the male tubal and ovarian factors, patient and her reproductive endocrinologist decide together on the optimal [fertility treatment options](#).

Factors to consider in selecting the best **fertility treatment options** include:

#### **Sperm source**

1. Is there a male partner: if so what is the ejaculate volume, sperm concentration, motility and shape? if >10 million moving sperm then pregnancy through intercourse or IUI is possible. Lower numbers indicates **IVF** or ICSI. If azospermia (no sperm in the ejaculate) then surgical sperm retrieval may be needed (TESE) or donor sperm can be used.

2. If there is no male partner: anonymous or known donor sperm is used

### **Tubal Factor**

1. Open fallopian tubes allow for natural conception or IUI.
2. Blocked fallopian tubes require IVF. Sometimes tubes can be fixed using tubal surgery.
3. Blocked and dilated fallopian tubes (Hydrosalpinx) require surgical removal of the dilated tubes followed by IVF. Dilated tubes are very difficult to fix and can leak fluid into the uterine cavity and prevent implantation of the embryo.

### **Ovarian Factor**

1. Women who do not ovulate due to polycystic ovary syndrome (PCOS): ovulation can be induced using oral medications (clomid or letrozole) or injection medications (gonadotropins). This is usually combined with IUI.
2. Women who do not ovulate due to defect in the master gland in the brain (Hypothalamic amenorrhea): ovulation can be induced using injection medications (gonadotropins). This is usually combined with IUI.
3. Women diminished ovarian reserve and unexplained (idiopathic) infertility commonly have lower quality eggs and may benefit from inducing multiple ovulation followed by IUI or IVF, to increase the chance that one of the eggs is healthy (chromosomally normal).

### **Donor Eggs**

1. Donor eggs are needed in women with low egg reserve that fail multiple IVF cycles after menopause or those who carry some genetic abnormalities.
2. Donor eggs can enable same sex male couples parent a child (together with a gestational carrier).

## **Gestational carriers**

1. Gestational carriers enable women to parent a child if the uterus is absent or was removed due to a disease e.g endometrial cancer or if the lining of the uterus is damaged e.g intrauterine scarring due to prior scrapping.
2. Gestational carrier enable women who cannot get pregnant to parent a child e.g history of breast cancer
3. Gestational carriers enable same sex male couples to parent a child.

## **Genetic analysis of the eggs or embryos (PGD)**

1. Women and men with risk of conceiving a child with a specific genetic disorder e.g cystic fibrosis, sickle cell anemia should consider testing their embryos before transfer into the uterus (PGD)
2. PGD can also be used for selecting the sex of the baby for family balancing.
3. PGD can be used to test the chromosomes of the embryo to increase the chance for pregnancy in women select women but its efficacy for that purpose is still being investigated.

## **Fertility Preservation**

1. Women at risk for diminished fertility due to a medical problem or treatment e.g breast cancer can freeze their eggs or embryos to use later
2. Men at risk for azospermia due to genetic factors, cancer and cancer treatment can freeze sperm for use later
3. Many other techniques for fertility preservation can also be applied to adults and children to preserve reproductive organs and tissue.

Many [fertility treatment choices](#) exist to help women and men conceive a child. One or more of these methods can be tailored to each

*i. individual circumstances:*

singles women or men,

heterosexual couples or

same sex couples.

*ii. reproductive aim:*

wants to get pregnant now versus later,

wants one child only or accepts twins,

wants to conceive a child of certain sex,

will use own uterus or a gestational carrier,

will use own gametes- sperm or egg or donor gametes.

To learn more about [fertility treatment options please visit \[nycivf.org\]\(http://nycivf.org\)](#)

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**Idiopathic Infertility**  
**Treatment: what do you need**  
**to know**

# **Idiopathic Infertility Treatment: what do you need to know**

**Idiopathic infertility (unexplained infertility)** is defined as inability to conceive after trying for 6 months in women 35y or older and one year for women younger than 35, with no tubal, ovarian or male factor infertility. This diagnosis of idiopathic infertility is established after open fallopian tubes are detected in HSG or laparoscopy, regular ovulation is detected from history, lab tests and ultrasound and sperm is near normal on sperm analysis. These fertility tests can be performed within few days. Note that good health and physical fitness..etc are not factors here. Many women with terrible general health do conceive. On the other hand, many women in excellent physical fitness and sound health have extreme difficulty conceiving even with fertility treatment. Having difficulty getting pregnant without an apparent cause applies to a large category of the sub-fertile population and is puzzling to couples trying to conceive. The consensus of opinion among reproductive endocrinologist can divide the underlying factors for unexplained infertility into

## **1. Chromosomal abnormalities in the egg (low egg quality)**

Abnormal eggs are present in every woman, albeit to a varying degree. Older women has more abnormal eggs. In addition, the fewer eggs you have the higher the proportion of abnormal eggs. There is no *non-invasive test* for egg quality and history, age, blood tests for ovarian reserve and antral follicle count detected on vaginal ultrasound are the most used methods.

### **Factors that point to low egg quality**

1. Advanced maternal age,
2. Diminished ovarian reserve (e.g high FSH, low AMH), also

prior surgery in the ovaries, smoking, family history of early menopause and exposure to chemotherapy

3. Early pregnancy loss before a fetal heart activity is detected (chemical pregnancy, blighted ovum),
4. Abnormal chromosomes of the products of conception and
5. Abnormal chromosome configuration of male or female partner e.g chromosome translocation. Less than 5% of couples miscarry due to a translocation in the male or female partner.

2. Other factors: may be more prevalent in younger patient and include mild endometriosis, immunological factors as anti-sperm antibodies, abnormality in cervical mucus, abnormalities in the cavity of the uterus and endometrial lining. Generally, these are not considered major factors in idiopathic infertility. Mostly oral medication produce few or only one follicles, thus they do not increase the chance that one or more eggs are healthy leading to a pregnancy.

## **Treatment Options for Idiopathic Infertility**

### **Oral medication – IUI or expectant treatment (intercourse)**

Oral medications are either clomid (clomiphene citrate) or an aromatase inhibitor (mostly letrozole) are used. This is followed by intercourse or intrauterine insemination (IUI). The pregnancy rate is about 5% to 7% per treatment cycle. There is no evidence that oral medications followed by IUI are superior to just intercourse in treatment of unexplained infertility. The risk for multiple pregnancy is about 8%. However, because oral medication (clomid) widespread use, mostly without ultrasound monitoring, they are probably responsible for more multiple pregnancy than any other fertility treatment.

## **Injection medications – IUI**

This **treatment** should probably be avoided in the majority of couples because of a. No added benefit: Pregnancy rate is not significantly higher than Clomid-IUI cycles; 9% pregnancy rate per treatment cycle and drops to 5% in women >38y. b. Risks: notably multiple pregnancy (two or more babies; 30%) and higher order multiple pregnancy (three or more babies; 3 to 8%). Multiple pregnancy has significant risks to the mother and babies. Preterm delivery can be associated with permanent neurological and intellectual defects in the babies. This risk can be minimized with careful stimulation under supervision of a reproductive endocrinologist, but cannot be completely prevented.

## **In Vitro Fertilization (IVF)**

a. The pregnancy rate per an IVF treatment cycle is approximately 30% on average, three times that of IUI. The specific pregnancy rate is dependent on female age. The time to conception is also shorter than any other fertility treatment modality. The higher success rate can be further extended through the use of frozen embryos in couples that have good quality embryos available for freezing. The cumulative pregnancies resulting from fresh transfer and subsequent frozen-thaw embryo transfer can result in a very high odds for pregnancy. Frozen embryos can be used years after their creation, when ovarian reserve has considerably diminished. The contribution of IVF to treatment success becomes more pronounced in older women >38 years as the success of ovarian stimulation – IUI drops considerably. b. The risk for twins and higher order multiple pregnancy can be greatly minimized through single embryo transfer (1% twins and no higher order multiple pregnancy). In other words *if you want to get pregnant faster, with one baby and at higher chance for success per treatment cycle strongly consider IVF with single embryo transfer.*

# **Infertility Treatment Strategy for Idiopathic Infertility**

Conventional [fertility treatment](#): “expectant management → clomid / letrozole- IUI x2 to 3 cycles → gonadotropin – IUI x3 cycles → IVF ” is the old method of treatment for unexplained infertility Modern treatment of Unexplained infertility: ” expectant management or oral medication – IUI → IVF preferably with single embryo transfer “. Women 38 years and older modern treatment strategy suggests Immediate IVF as the initial fertility treatment. The modern paradigm for fertility treatment will lead to pregnancy faster, is more successful, minimize multiple pregnancy and is more cost effective (lower dollar cost per baby). The majority of women (>70%) with unexplained infertility especially women with normal ovarian reserve will succeed in delivering a baby.

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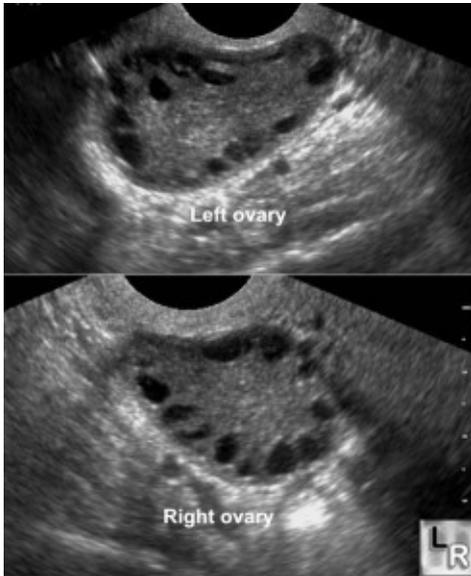
## **Letrozole vs Clomid for Ovulation Induction in PCOS**

### **Letrozole vs Clomid for Ovulation Induction in PCOS**

**Polycystic Ovary Syndrome (PCOS) is associated with two of the following criteria:**

- a. No ovulation (anovulation) or less frequent ovulation
- b. High male hormone (androgen)
- c. Polycystic appearance of the ovaries: large number of small follicles

**Clomid is an oral medication that modulate or mask the estrogen receptor leading to release of internal FSH from the brain**



Polycystic Ovary

**Letrozole is an oral medicine that reduces estrogen production from the ovary through antagonizing the function of the aromatase enzyme, responsible for making estrogen. The brain respond by releasing FSH.**

**Which one is better?**

In a recent good quality study, 750 infertile women, aged of 18-39 years, with a diagnosis of PCOS were studied. The women were randomly allocated to CC vs. letrozole for 5 treatment cycles. CC 50mg every day for 5 days (days 3-7 of cycle), or B) letrozole 2.5mg every day for 5 days (days 3-7 of cycle), for a total of 5 cycles or 25 weeks. The dose will be increased in subsequent cycles in both treatment groups for non-response or poor ovulatory response up to a maximum of 150 mg of CC a day (×5 days) or 7.5mg of letrozole a day (×5 days). 27.5% of women who received letrozole (Femara) had a live birth, compared with 19.5% of women treated with

clomiphene. One quarter were clomid resistant and never ovulated.

Letrozole was associated with lower multiple pregnancy rates.

Letrozole appears to improve live birth and pregnancy rates in subfertile women with anovulatory PCOS, compared to clomiphene citrate.

Letrozole should be considered as a first line agent for induction of ovulation in women diagnosed with PCOS.

In general it is advised that oral medication are tried first in PCOS before proceeding to injection medications (gonadotropins). Gonadotropins induce multiple ovulation and increase the risk for multiple pregnancy. If oral medications fail to induce ovulation or no pregnancy ensues, it is preferable to proceed to IVF with single embryo transfer and not injectable medications – IUI to avoid twins and higher order multiple pregnancy.