Ovarian Reserve Revisited-Do You Have Enough Good Eggs?

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Trying to conceive over age 35 is generally not easy

I know because I tried for years to have a baby without success. While there are many factors which impact conception, one of the first concerns for women over 35 is if they have enough healthy eggs to get pregnant. Research has shown that women carry a reserve of eggs throughout their lives and that reserve diminishes over time. There are several tests which help to determine ovarian reserve including antral follicle testing, the clomid challenge and the AMH test which is relatively new.

The antral follicle test

Uses vaginal ultrasound to count and measure the small follicles, antral follicles, on the ovary. The higher the number of antral follicles, the better ovarian reserve and better odds for conception.

The AMH Test

Anti-mullerian hormone test, measures the levels of AMH in a woman’s blood. Since this hormone remains relatively constant over the menstrual cycle, it can be tested at any point in the month. Women with higher AMH levels tend to have a better ovarian reserve and a better chance at conception.

When I decided to try to conceive one last time at age 44

My reproductive endocrinologist began by ordering the *Clomid Challenge Test*. For the test, I took clomid, a fertility drug used to induce ovulation, for 5 days. Generally speaking, the procedure works like this:

- On Day 3 of your menstrual cycle, a blood test is given to measure your FSH, LH, and estradiol levels.
- On Day 5 of your cycle, you begin to take a 5-day supply of clomiphene citrate, 100 mg of clomiphene each day for five days.
- On Day 10, you will have another blood draw to check FSH, LH, and estradiol levels again.

Normal results include low FSH values on both Day 3 and Day 10, and low estradiol values on Day 3. Results are abnormal if your FSH values are elevated. Your doctor may decide to re-test if your results are abnormal.

My results were normal but that is a fraction of the total conception story and half of the ovarian reserve story. Ovarian reserve consists not only of the quantity of eggs but also the quality of eggs. Research tells us that while tests like the clomid challenge check for the quantity of eggs, the quality of eggs is generally determined better by age. This is an unfortunate fact for those of us over 35.

According to Dr. James Toner in his paper "Ovarian Reserve, Female Age and the Chance for Successful Pregnancy", once women reach their mid thirties, specifically 37, their egg quantity begins to diminish at a faster rate. Tonor also reports that even if egg quantity is good, chances of a viable pregnancy drop due to the diminishing quality of eggs as women age.

Based on the research, it is clear that the averages do not

look promising for women over age 35 trying to have a baby. There is, however, other information to consider. Let's take a look at the bell curve. Basically, about 2/3 of the cases for a given situation fall in the fat part of the curve meaning that averages generally apply to most people. However, there are still one third of the people who fall outside of the fat part of the bell curve and averages do not generally apply to them. As you look at your individual situation, it is your lab work, anatomy and physiology that matter. I am a classic example of defying the odds. My ovarian reserve quantity was good but that wasn't what was preventing me from conceiving a child. It took many more tests to determine that a badly placed uterine tumor was most likely preventing implantation. At age 44, the research showed that an average woman in my situation had only a 3% chance of having a healthy baby. Yet, I was able to conceive in two of 4 IUI treatments and gave birth to a healthy little girl 9 months ago at the age of 45.

There are many components to conceiving a child

Ovarian reserve is one of them. There are also many medical interventions to boost the odds of conception. Medical research provides us with excellent information about infertility and age including work on ovarian reserve. While the research tells us that the odds of getting pregnant in late 30's and 40's diminishes, one needs to remember that each woman is unique and she needs to work with her doctor to explore all options in her quest for pregnancy.

About the Author: Deborah Lynn is the creator/owner of Over 35 New Moms and a former corporate vice president. She holds degrees in Education, Kinesiology and pursued doctoral study in Physiology. She spent over 17 years working in the corporate environment and now focuses her time on raising her daughter and helping other women over 35 in their

journey to have a baby. For more information, visit The Resource Guide for Pregnancy over 40 at http://www.selfgrowth.com

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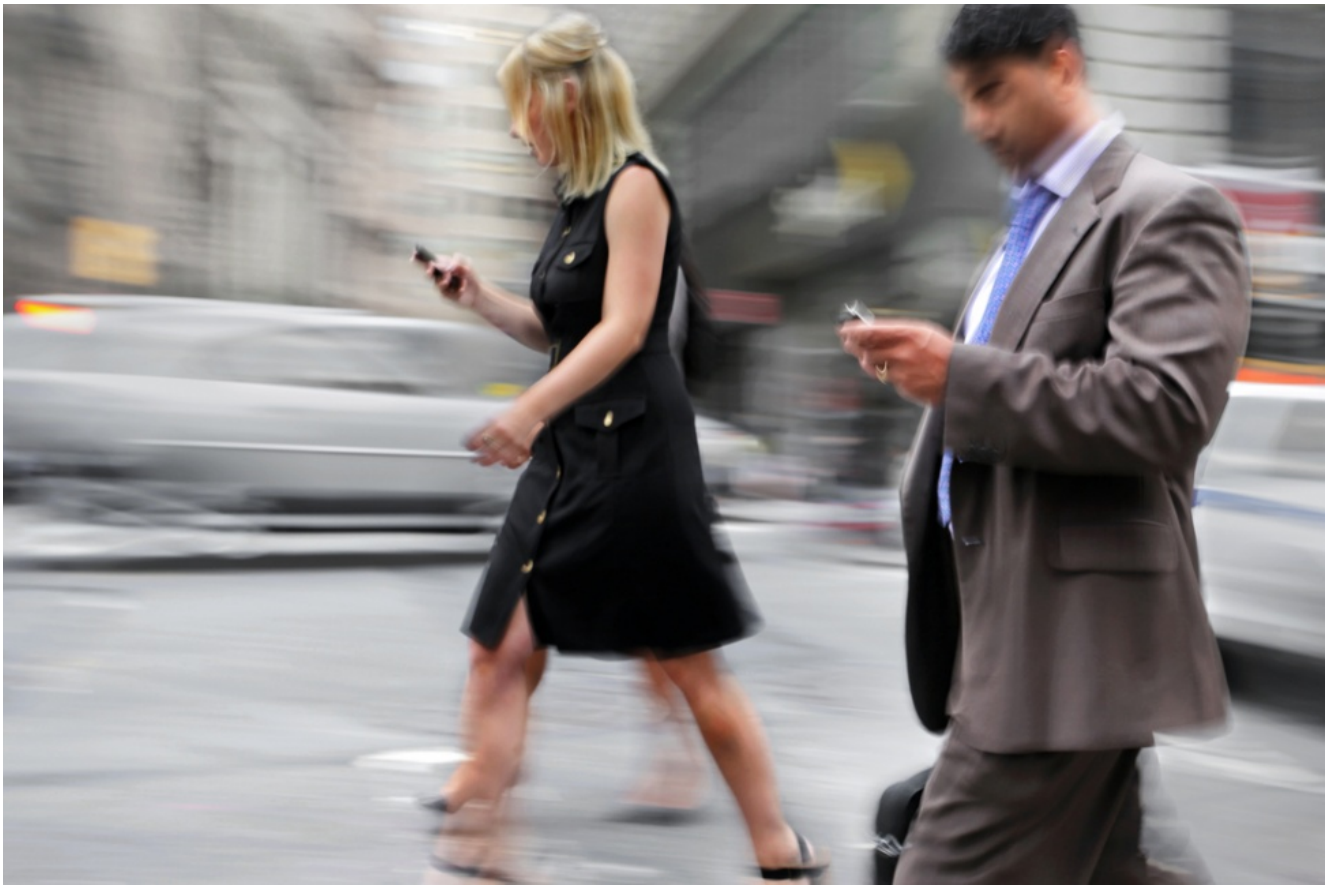
Fertility Treatment: Do not be Distracted



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 6months 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 there simple logic. They can lead to delay in fertility testing and fertility treatment that could be detrimental to future fertility.

Trying to Conceive (TTC): What Does Timed Intercourse Means?

If you are trying to conceive (TTC) there is one thing you need to do as it is very helpful in achieving a pregnancy.

There are also few things that are not very helpful.

Timed Intercourse : How to do it?

The majority of pregnancies take place when intercourse takes place in the six day and especially two day period ending in the day of ovulation (fertile window). Some advice that

ovulation should be timed using cervical mucus, basal body temperature or urinary luteinising hormone (LH) kit. Several factors are against this approach:

1. Timed intercourse is emotionally stressful
2. Sperm survive in the cervix, uterus and fallopian tubes for several days (>3 days, close to 7 days)
3. Studies that evaluated the use of mucus, BBT or LH kits to time intercourse did not report better odds for natural conception.

The best approach to a timed intercourse is not to time it at all provided that sex is frequent enough to maximize the chance for sperm-egg interaction. Intercourse three times a week appears to optimize the chance for natural conception.

It is not true that frequent **intercourse** reduces the pregnancy rate due to reduced sperm count and quality.

Timed Intercourse : How long?

Approximately 85% of women trying to conceive conceive within the first year. The American Society for Reproductive Medicine recommend seeking consultation if pregnancy does not ensue after one year of intercourse in women younger than 35 years and six months in women 35 years and older.

The limited Value of Cervical mucus, BBT and LH kits

Cerivcal mucus, BBT and LH kit are not accurate methods to **time ovulation**. Fluid cervical mucus, rise in temperature and positive urine LH can take place without ovulation or several days before ovulation. Studies evaluating these methods did not find and increased chance for pregnancy. Using a calender or *App* to register symptoms and mucus was not scientifically evaluated.

For a minority of couples that cannot have frequent sex (every 2 to 3 days) the use of LH kits maybe helpful. All the other methods (mucus, temperature) had less than 50% correlation to ovulation.

Fertility Apps

Fertility Apps

Fertility apps are generally not helpful in enhancing fertility because they are not based on scientific information. The premise that cervical mucus character, urine LH kit and BBT charts are better than frequent intercourse is not scientifically correct. Thus apps based on tracking ovulation cannot contribute to your fertility beyond intercourse three times a week. No app so far was scientifically tested and was shown to enhance fertility in women or men.

Conclusion: Do have intercourse three times per week after the end of bleeding days. Do not time intercourse. If you must use

urine LH kit. If you do not conceive in 6 months (≥35y) or a year (<35y) consult with a reproductive endocrinologist. Throw your iphone or keep it and delete the app (till a truly helpful app is available).

Egg Quality and Fertility Treatment Success

What does egg quality means?

Good quality eggs are mature eggs that are able to fertilize, develop into normal embryos that are able to implant and progress to a healthy baby. Good **quality eggs** have normal chromosomes. A normal egg contains 23 chromosomes and when fertilized with a sperm produce a zygote that has 46 chromosomes.

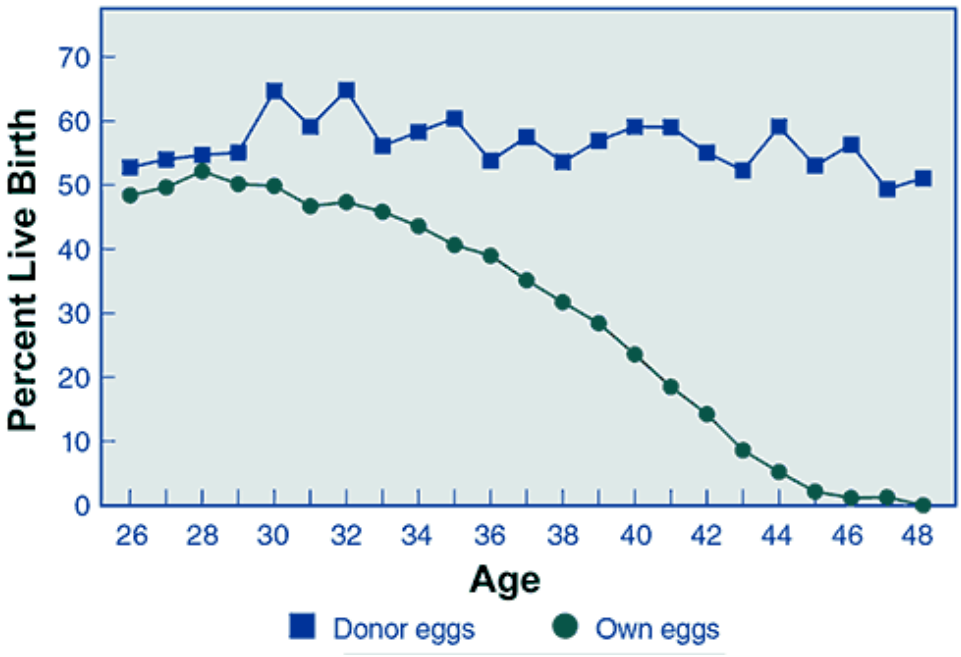
How is egg quality tested?

Two methods

1. Non invasive: asking a woman about her age. Age is the most important determinant of fertility. All women have abnormal eggs and well as normal ones. With advance in age the proportion of normal eggs decrease because the ovary ovulates the healthier eggs earlier in life. Older women have less eggs and more abnormal eggs. Apart from age and ovarian reserve testing there are no other noninvasive methods to test for egg quality. Couples may present with unexplained infertility, minor abnormalities or repeated unsuccessful **fertility**

treatment. Other indicators of lower egg quality are recurrent early first trimester pregnancy loss (biochemical pregnancy), pregnancy loss in the first trimester when chromosome analysis of products of conception is abnormal. Ectopic pregnancies are more common with chromosomally abnormal embryos.

2. Invasive method: the eggs can be retrieved and DNA analyzed via PGD, before or after fertilization to detect the number and structure of chromosomes. This is usually done during actual fertility treatment.



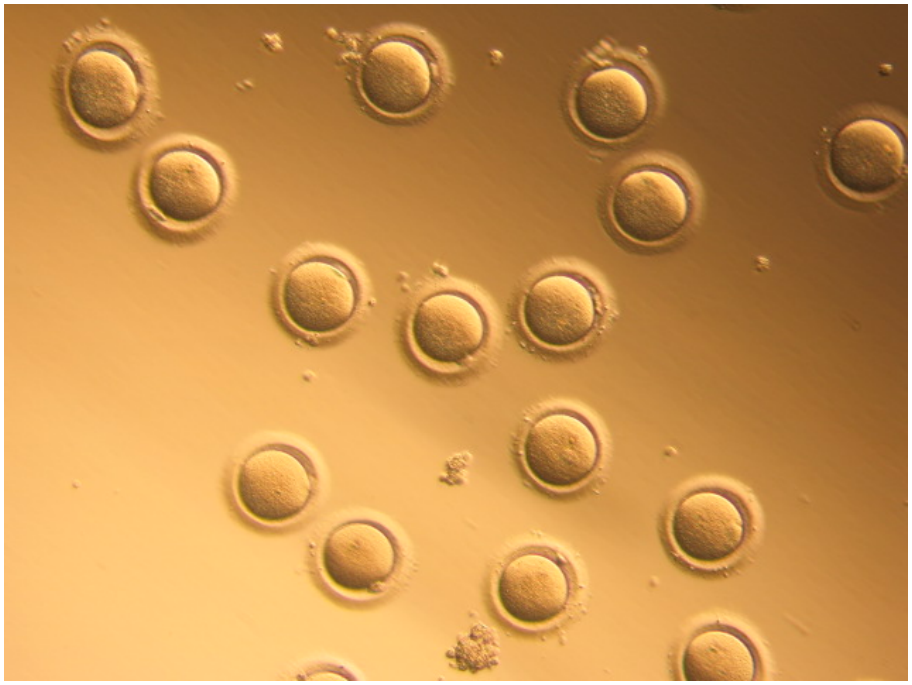
Advance in maternal age is associated with lower chance for conception due to lower number of eggs with normal chromosomes

How can we improve egg quality during fertility treatment?

Strategies employed to improve **egg quality** during **fertility treatment** include

1. **Random increase in the number of eggs produced**: Ovarian

stimulation can increase the number of eggs produced increasing the odds that one or more of those eggs have normal chromosomes. This random increase in the number of eggs is employed in IUI and IVF cycles. We do not know if any of the eggs are normal but generally the more eggs you make the higher the likelihood that one or more are normal.



Human eggs retrieved after ovarian stimulation

2. **Tweaking of ovarian stimulation protocol**: Many changes to the stimulation protocol can improve response and egg quality including, choosing an agonist or antagonist based protocol, the addition of an oral agents like clomid or letrozole, reducing the dose of gonadotropins, changing the timing for the trigger shot hCG.
3. **Embryo selection using morphology**: Healthy embryos divide and double the number of cells every 24 hours or less (8 to 10 cells on day 3). Healthy embryos have equal cells and each has a single nucleus. Healthy embryos are not fragmented (due to cell breakdown). These embryos are identified under the microscope. The problem with morphology is that many unhealthy embryos

are good looking. the prediction ability of morphology in detecting chromosomally normal embryos is probably 60% or less. Morphology, however is non invasive and cheep. Extended vulture is used to push embryos to day 5 to observe which embryo will reach the blastocyst stage and select it for transfer. Blstocysts have generally higher implantation rates than day 3 embryos because of the ability to select the better embryos. Extended culture is employed when many embryos are available on day 3 (usually five or more).

4. **Genetic analysis of eggs or embryos**: The most important point to know about genetic analysis of eggs and embryos is that PGD does not create a new potential or improve the overall success for fertility treatment for a given stimulation cycle. It just detects fairly accurately (not 100% accurate) the chromosome makeup of eggs or embryos. The potential advantage of PGD is to directly select the embryo, out of available cohort, that is most likely to implant instead of selecting based on morphology. Thus it maybe helpful for women with large number of embryos available on day 3 and day 5. In other words if you have two embryos available on day 3 and you are transferring two embryos, there is no point in testing them. On the other hand if you have eight embryos on day 3 and you will only transfer 1-2 embryos, then PGD may makes sense to go directly to the embryos most likely to work.

The potential disadvantages of PGD are the need for embryo biopsy that potentially may harm the embryo. PGD assumes that the cell obtained represents the whole embryo while sometimes that cell chromosomes maybe different than the embryo. The method for analysis used is not 100% accurate. In other words the method may misdiagnose a healthy embryo as abnormal or vice versa or on occasions fail to diagnose the embryo at all. PGD is expensive requiring embryo biopsy and embryo genetic analysis.

So far no large scientific studies are available and reproduced by many centers indicating increase in fertility potential of IVF. Because of all these factors, PGD is selectively applied to select patients and not a universal step in all IVF cycles.

Other methods suggested as supplements as well experimental methods as mitochondrial transfer still lack scientific evidence that they work.