

# Ten Reasons why You Should not Use Clomid for Fertility Treatment

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### **Not the Way your Using it Anyway**

*Ten Reasons why You Should not Use Clomid for Fertility Treatment, Not the Way your Using it Anyway.* Clomiphene citrate (clomid) was the first medication introduced for fertility treatment (1960s). It works through masking of estrogen receptors in the brain. The brain, blind to estrogen in the blood, starts pouring FSH, the protein that drives development of dormant follicles in the ovary.

When one considers a fertility treatment: not only the pregnancy and delivery rates per cycle is considered, but also the time to conceive (TTC) and the complication rate especially multiple pregnancy. Clomid is a very attractive medicine to women and gynecologists, alike. It is an oral medication, easy to use for both general gynecologists and women seeking fertility treatment. It is also cheap. It is successful in inducing ovulation in 90% women that do not regularly ovulate e.g. polycystic ovary syndrome. Response to clomid is modest in most cases (1-2 follicles).

In spite of all these advantages, there are many other disadvantages. It, most likely, will not improve the odds of conception in regularly ovulating women. Its indiscriminate use, in The US and worldwide (without ultrasound monitoring of ovarian response), probably makes clomid the drug responsible for multiple pregnancies over all other forms of fertility treatment. Although clomid is successful in inducing ovulation

in 80-90% of well selected patients, only 20% become pregnant. This discrepancy happens because of undesirable effects of clomid on the lining of the uterus (thin) and cervical mucus (thick). In my opinion though, many clomid cycles fail due to its in women that are not destined to benefit from it. Those are older and regularly ovulating women with unexplained infertility as opposed to suitable candidates: younger non-ovulating women. Clomid offers little help to women with unexplained infertility (ovulating) because in these women, the majority do not conceive because of chromosomal abnormalities in the eggs. Clomid commonly does not induce superovulation (many follicles) to partially compensate for abnormalities in the eggs.

## **Do Not Use Clomid Unless**

1. Preconception labs are normal. Many patients are prescribed clomid without a complete fertility workup, including genetic screening. If you and your partner are carriers of cystic fibrosis or sickle cell anemia gene abnormalities, for example, you are at risk of transmitting these diseases to your future children (1:4). Genetic screening should be performed BEFORE starting fertility treatment. It does not help you to detect these abnormalities after pregnancy ensues. Decline clomid or any other fertility treatment without proper preconception history and lab tests.

2. Evidence of patent tubes. After ovulation induction, using clomid, the eggs has to be picked up by the fallopian tubes. Sperm also has to enter the fallopian tube to allow fertilization. Completely blocked fallopian tube may prevent the egg and sperm to meet. Partially blocked fallopian tube may allow fertilization but the the embryo may become stuck in the tube leading to ectopic pregnancy.

3. Near normal sperm analysis. A sperm concentration of < 15 million per mL and movement < 50% may reduce the odds for fertilization and reduce the chance of pregnancy after clomid

treatment.

4. If you ovulate regularly. Together with normal sperm analysis and open tubes, that indicates you have unexplained infertility. The most likely cause for not conceiving is chromosomal abnormalities in the eggs. We cannot fix chromosomal abnormalities in the egg but we can induce the ovaries to produce more eggs. More mature eggs means more chance of producing a normal egg. Clomid induces the ovary to produce 1-2 eggs in most cycles, thus does not address effectively egg abnormalities. On the other hand, if you are young and do not regularly ovulate, clomid is able to induce ovulation and potentially solve your problem.

5. Without monitoring. Some women are more sensitive to the effects of clomid. They respond by producing a large number of follicles. The safest approach here is to cancel the cycle and restart another treatment with a lower dose. Although the risk of multiple pregnancy with clomid is about 10%, women that respond with producing a large number of follicles are at a much higher risk. Careful monitoring of response, using vaginal ultrasound, is required in all clomid cycles.

6. Use the lowest dose that leads to ovulation (start with one tablet per day). Do not increase the dose if ovulation took place at a lower dose. Most patients get pregnant at doses of 50 to 150 mg (1-3 tablets) per day. Increasing the dose does not increase the chance for pregnancy and increases the side effects of clomid e.g thin endometrium, thick cervical mucus..

7. Do not use clomid more than 3 months (6 months life time max). The majority of women get pregnant in the first three months of treatment. If you are younger and ovulate on clomid and would like to try few more months, then 6 months is the maximum amount of time you should use clomid in your life time.

8. Clomid less likely to lead to pregnancy delivery in women

>38y. In women 38 or older with unexplained infertility, there is good evidence that clomid-IUI is inferior to IVF. The vast majority of women in that age group that start on clomid end up switching to IVF to achieve pregnancy.

9. Expertise with optimizing clomid cycles: clomid cycles should be supervised by a physician with expertise in clomid dosing, use of repeat courses, use of adjuvant treatments as estradiol and IUI. This enables maximizing the benefits of fertility treatment and tailoring treatment to individual woman.

10. Use letrozole before using clomid. Accumulating evidence from many studies, including randomized clinical trials, indicates that letrozole is superior to clomid in terms of achieving pregnancy. Applying the same principals above, letrozole should be considered as the initial treatment for anovulatory infertility.

## **On tailoring Fertility Treatment to Specific Patient's Needs**

In too many times, the use of clomid for fertility treatment is a stark example of tailoring patients to treatments familiar to general gynecologists, rather than individualizing fertility treatment to women biology and fertility needs, citing ease of use, perceived safety and familiarity. Cheap treatments that appear safe can quickly become aggressive and unsafe if they lead to low pregnancy rate and high multiple pregnancy. The time lost treating older patients with clomid for a prolonged periods can be detrimental to their ovarian reserve and can minimize the chance for eventually achieving pregnancy and delivery.

## **On men and clomid**

There is no proof that men benefits from the use of clomid and similar treatment to improve sperm parameters. Specifically, there is no evidence that female partners of men that were

prescribed clomid conceive at higher rates. With very few exceptions, clomid should not be used to treat male factor infertility.

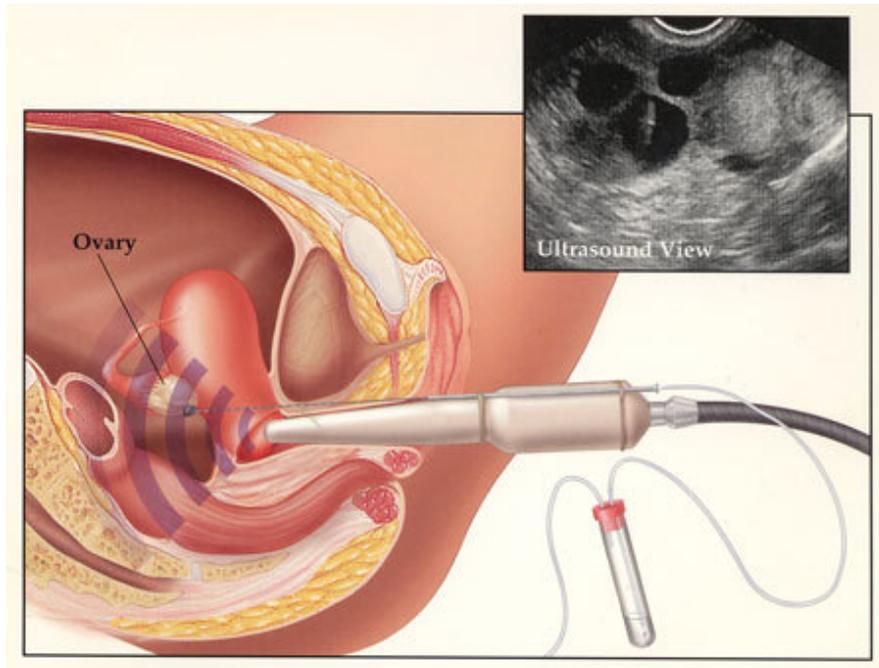
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## **IUI or IVF for Unexplained Infertility**

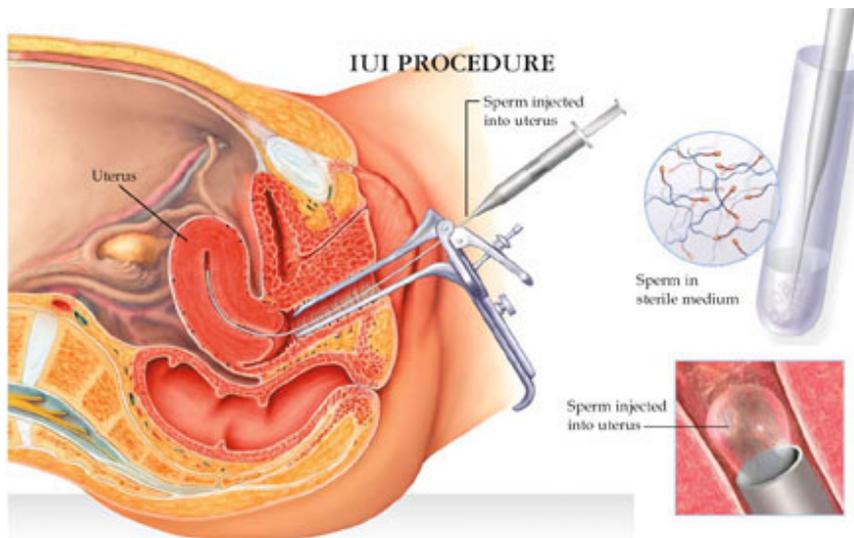
Choosing IUI or IVF for unexplained infertility can be confusing. If you have been trying to conceive for several years and initial fertility tests does not reveal any abnormalities (open fallopian tubes, normal sperm and regular ovulation), you will be diagnosed with unexplained or idiopathic infertility.

**Possible treatments include ovarian stimulation-IUI or IVF**

**What should you consider before deciding between IUI and IVF?**



IVF In Vitro Fertilization



Intrauterine Insemination (IUI)

1. Pregnancy rate: IVF is associated with higher pregnancy rate than IUI, approximately 3 times. In women less than 35 pregnancy rate is approximately 50% with 2 embryo transfer and 35% with one embryo transfer versus 10-15% per one cycle of IUI.
2. Multiple pregnancies: When ovulation is stimulated using injection medications (FSH) the chance for twins is

about 30% and higher orders multiple pregnancies 1-3%. Multiple pregnancies is associated with increased risk of preterm delivery with possible long term effects on the newborns. Compared to IVF with single embryo transfer, the chance for twins is 1% and higher order multiples is very low. Actually IVF with single embryo transfer is the more conservative approach in women at risk for multiple pregnancies with IUI.

3. Cost: IVF is more costly due to the requirement of lab procedures to fertilize the eggs and culture the embryos. If multiple pregnancies at it complications are factored in IVF with single embryo transfer appears to be the cheaper approach.

Sound evaluation by a reproductive endocrinologist can give you the advice and guide you through the decision.

Women with high ovarian reserve as PCOS are better served in general by avoiding injection medication + IUI and proceed to IVF if oral medication e.g clomid do not succeed. Women with reduced ovarian reserve generally will have a high odds for getting pregnant with IVF than IUI.