



CYCLE EVALUATION

In order to evaluate how well you ovulate, we will see you on three days during your menstrual cycle. Early in the cycle you select a dominant follicle, on or about the third day of your period. Your first appointment will be "**Day 3**". You should ovulate mid-cycle. Your second appointment will be the day after you see a color change with the ovulation predictor kit, or "**Day 14**". The third important day is the day of implantation approximately "**Day 21**" of an idealized 28 day cycle.

During this evaluation, we will draw blood to measure hormone levels, and perform (vaginal) ultrasounds to measure follicular dimensions and endometrial lining thickness.

Please review this guide carefully.

I. Early In Cycle

A. Selection of the Dominant Follicle (~ Day 3)

Call the office, preferably in the morning, once you are certain that you are having true menstrual bleeding (not just spotting). **Please call the office on the first day of your cycle. We will see you on Days 2 - 4** of your menstrual period for an **ultrasound examination**.

If this is your first cycle, we will draw baseline labs such as estradiol (**E2**), follicle stimulating hormone (**FSH**), lutenizing hormone (**LH**), and progesterone (**P4**) levels to help determine ovarian reserve. This will assist in determining how much help you may need with ovulation. We will also draw a thyroid stimulating hormone level (**TSH**) and thyroid peroxidase antibodies (**TPO**). If you do not have a record of your blood type and Rh factor or rubella immunity, these will also be drawn.

B. HSG X-RAY

If you need to have a **hysterosalpingogram** (HSG), we will help schedule this **x-ray** for you at the time of your Day 3 visit. The x-ray itself is done after your menses has stopped, but between Day 7 - Day 10 of your cycle. We will also give you a prescription for an **antibiotic** which you should **start the day before the test**. More detailed instructions will be given to you on your Day 3.

C. Ovulation Induction

Oral Medications

Each cycle you initially awaken as many a dozen follicles, and then select from this group a single dominant follicle which contains a single egg to result in a single offspring. All large mammals do this.

Follicle Stimulating hormone (FSH) is the fuel that drives ovulation. At the very beginning of your cycle, your FSH will rise to whatever level is needed to start the next group of follicles. Your brain senses that this process has started when it begins to detect rising levels of a special estrogen, called estradiol (E2). Once this estrogen is detected, your brain responds by cutting back on the amount of FSH, or fuel, it produces. This gradual decrease in fuel causes all but the strongest follicle to stop.

In your consultation, you will learn about the dynamic feed-back loop between the brain and ovaries that silently runs in the background regulating ovulation. Once it was understood that increasing estrogen early in the cycle results in a fall in the brains production of fuel (FSH), researchers discovered that hiding or depriving the brain of estrogen causes the level of fuel to shoot up. **Clomiphene citrate** (also known as Serophene® or Clomid®) works by hiding estrogen receptors. **Letrozole** (Femara®), blocks the production of the active form of estrogen. Given for a short period, early in the cycle, either will cause Follicle Stimulating Hormone rise. This increase in FSH "super charges" the cells which surround and nurture the egg, and cause the mildest "super ovulation."

1. Clomiphene citrate

If you are scheduled to receive **clomiphene citrate**, we will see you Day 2-4 of your cycle, and perform a vaginal **ultrasound** to determine if your ovaries are "clear." It is important to know that there is no evidence of **residual cysts** which might make stimulating ovulation dangerous. At that time, you will receive a prescription for the medication. The generic clomiphene citrate, works equally well as either of the brand name drugs Clomid® or Serophene®.

We generally give this medication cycle Days 3- 7. You should take the clomiphene approximately the same time each day. You may take this medication on an empty stomach or with a light meal.

Side-effects are rare at the doses we prescribe, but some patients may experience "**hot flashes**." Clomiphene works by blocking estrogen receptors, and can mimic the true absence of estrogen seen in the menopause). Ironically, it was initially developed as a contraceptive.

A few patients also report **headaches**. The headaches associated with this medication occur while you are taking the drug, and are generally responsive to Tylenol® or Advil®. Although we discourage taking aspirin-like medications around the time of ovulation, it is fine at this time.

2. Letrozole (Femara)

Letrozole was developed to treat breast cancer. It prevents the conversion of weaker estrogen precursors to the most potent estrogen, Estradiol, (E2). Ovulation induction with letrozole works in a similar fashion as with clomiphene, but by a different chemical process. Letrozole has a shorter serum half-life. (It leaves your system faster.) This results in fewer side effects, but also makes it a slightly weaker drug for ovulation induction. It is clearly beneficial for patients who have thin endometrial lining.

The cycle begins the same way, with a vaginal ultrasound cycle Days 2-4, and base-line labs. Letrozole is also taken cycle Days 3-7. On cycle Day 12, you return for an ultrasound and labs to see if the medication has captured one or more follicles, and to help us estimate when you will ovulate.

Injectable Medications / Gonadotropins

Some ovulatory problems do not respond to either clomiphene or letrozole. In other cases, certain patients are so sensitive to any estrogen blocking they can't tolerate these medications. The most direct way to increase follicle stimulation is by directly injecting Follicle Stimulating Hormone (FSH).

There are two popular FSH preparations, Follistim® and Gonal F®. Both are given via a "pen" delivery system - like an Epi-Pen. Follistim® and Gonal-F® are both synthesized entirely in a laboratory by recombinant DNA technology, and contain pure FSH.

Menopur® is highly purified "menopausal gonadotropin" (hMG) which contains both FSH and LH. Some patients do not make LH on their own and need both gonadotropins to achieve adequate ovulation.

Ovidrel® is a preparation containing human Chorionic Gonadotropin (hCG). As you will learn in your consultation, hCG can be used to stimulate or augment ovulation. This shot is often referred to as the "trigger" shot, as it triggers ovulation. Ovidrel comes as a prefilled syringe.

All of these medications are administered as a subcutaneous injections. Before starting these medications, you will need to schedule a **teaching session** with a nurse. The sessions are private and take approximately 30 to 45 minutes.

II. Mid-cycle Testing

A. Detecting Ovulation

During your evaluation we recommend using **Clear Blue Easy®** ovulation predictor kit. There are 16 different kits available commercially. When tested side-by-side, this kit appears to be the most sensitive and specific. A positive color change will indicate that ovulation will occur within **12 to 36 hours**.

Most patients will ovulate seven days after the last clomiphene or letrozole dose. We generally ask patients to **begin testing with an ovulation predictor kit beginning on day 11 of the cycle** (four days after the last dose). You should avoid taking anti-inflammatory drugs (aspirin, Advil®, Tylenol®) which may block ovulation. Similarly, avoid antihistamines (including Allegra® and Claritin® which decrease cervical mucous production around the time of ovulation). If you have seasonal allergies (hay fever), or chronic sinus problems, we will either prescribe sinus medication which doesn't affect reproduction, or refer you to an appropriate specialist.

It is best if you **test in the mid-morning**, at approximately the same time each day. These kits have been simplified so that they can be done at work or on the go. Please call our office with the **first sign of a color change**. Certain patients will not achieve a color change of greater or equal intensity to the reference line. **If you have not noted any color change in the test spot by Day 13 of the cycle, please call our office to schedule an ultrasound examination the next day, Day 14.** We can frequently determine what is blocking ovulation and begin corrective treatment.

If you are being stimulated with the injectable gonadotropins, part of the monitoring involves measuring LH in your blood stream. You will not need to use a urine LH kit in these cycles.

B. Abstinence

Please abstain from intercourse from the day you begin testing for the LH surge (usually Day 11). This period of abstinence will help to assure that your husband has a sufficient time to restore his sperm count. **Two to three days of abstinence is generally optimal.** If your specific circumstances are different, we will discuss optimal timing for you.

C. **Intrauterine Insemination (IUI)**

If we are planning to do an **intrauterine insemination (IUI)**, when you call with your color change, you will receive **two appointment times**. The first appointment will be the time for your husband to be at our office for his semen collection. The second appointment will be the time for your insemination.

Under certain circumstances, it may be necessary or preferable to collect the semen specimen at home. You will need to stop by the lab to pick up a **sterile specimen container** and the appropriate paperwork.

The insemination begins with an **ultrasound** to determine which ovary is ovulating. We will **direct the insemination catheter** to that side. We can also see if ovulation has already occurred or is in progress. If there is clear evidence of ovulation, we do a single insemination. If ovulation has not yet fully occurred, we will schedule a second insemination the following day. After the insemination, we have you rest for 20 minutes to allow the sperm time to swim through the fallopian tubes. After your insemination, there are no specific restrictions regarding activity or intercourse.

III. **Mid-Luteal Progesterone / Implantation**

One week after ovulation (eight days after your color change) is the approximate time of implantation. A **progesterone** level of **15 ng/ml or greater** is necessary to sufficiently mature the uterine lining for successful implantation. A prolactin level may also be checked at this time if indicated.

Direct evidence of endometrial maturation is obtained by means of an **endometrial biopsy**. This test is generally reserved for women with a strong history of implantation failure or recurrent miscarriage.

IV. Early Pregnancy

If your period has not started when expected, (this usually means within 28 to 32 days), we will do blood tests for the pregnancy hormones **β-hCG** ("beta" - human chorionic gonadotropin) and **progesterone**. β-hCG is actually produced by the placenta, not the embryo, and the level should approximately double within 48 hours. Your progesterone level should be maintained above 20 ng/ml. Supplemental progesterone is given if necessary.

Approximately **6½ weeks** after your last menstrual period, the embryo is visible by ultrasound. We should also be able to see the heart beating (called "fetal cardiac motion"), although some biologic variability is common.

Two weeks later, during the **eighth week** of pregnancy, the embryo should clear 18 mm in length (called the "crown-rump length"). Miscarriages after this point are rare. Once you have **safely cleared the first trimester**, we will transfer your care back to your initial obstetrician, or help you to find an appropriate obstetrician if you do not already have one.

Approximately one third of all clinically recognized pregnancies are complicated by some **spotting**. While progression to frank bleeding is obviously a sign of trouble, minor spotting is frequently simply the result of being too active early in the first trimester. Most of the time, **rest and adequate hydration** will allow this bleeding to stop.