



## PATIENT'S FACT SHEET: **CLOMIPHENE**

Clomiphene is a widely-used medication which stimulates the ovaries by making the pituitary gland increase its output of follicle stimulating hormone (FSH). It may be prescribed to treat fertility problems related to abnormal ovulation, or it may be prescribed to accomplish a clomiphene challenge test (CCT) which is a test done to measure the ability of the ovaries to respond to FSH. Clomiphene is the generic name of the medication; Clomid® and Serophene® are two brand names.

During a menstrual period, estrogen levels become very low, and this triggers the pituitary gland to produce FSH to stimulate the ovaries to make egg follicles grow. The ripening egg follicles make estrogen. When the estrogen levels get high enough, and the egg is "ripe," the pituitary gland makes a second stimulating hormone, leuteinizing hormone (LH), which causes the egg to be released so that it can be fertilized. After ovulation, the lining of the egg follicle becomes the corpus luteum, and produces progesterone which prepares the uterine lining to receive the fertilized egg. If there is no pregnancy, the progesterone production stops after about two weeks, and this triggers the uterine lining to be shed, resulting in a period. If pregnancy occurs, the corpus luteum continues to produce progesterone, which is important to the developing pregnancy, for about two more months, after which the placenta takes over progesterone production.

Clomiphene is given shortly after menstruation. It "jump starts" the cycle by tying up the estrogen binding sites in the pituitary; the pituitary gets a reading of lowered estrogen and responds by sending out increased FSH. The increased FSH results in better follicle production, which in turn should lead to increased estrogen and progesterone levels during the cycle. Women who don't ovulate may ovulate, and women who don't make enough progesterone after ovulation (luteal phase defect) may have an improved cycle, with a better ovulation and a better corpus luteum making more progesterone.

During the first clomiphene cycle, we may do some type of monitoring for response, but no adjustments can be made once the cycle is started. Monitoring may consist of doing a basal body temperature (BBT) chart to track ovulation, or monitoring blood levels of progesterone in the luteal phase. An ultrasound around cycle day 11 can demonstrate whether follicles are developing. Measuring the number and size of follicles can help to judge response. Release of eggs from the follicle(s) can be triggered by giving an injection of HCG which mimics the normal LH surge. Generally the follicle(s) will release 36-42 hours after the HCG is given. Timed intercourse or intrauterine insemination (IUI) can then be planned. We may or may not need to do monitoring when clomiphene is taken during subsequent cycles.

The dose of clomiphene may need to be adjusted to achieve the desired response. We generally start with the lowest dose (50 mg daily, day 5 through 9 of a cycle). If the desired effect is not achieved, then the dose will be adjusted upwards in a *subsequent cycle*.

When doing a clomiphene challenge test (CCT), we use the medication to see how well the ovaries respond to stimulation. We will check blood levels of FSH and estrogen on day 3 of your cycle (just before taking the medication) and again on day 10 (just after taking the medication) to accomplish this. Even though the CCT is designed to be *diagnostic* rather than *therapeutic*, pregnancies sometimes occur during that cycle due to the stimulation of the ovaries. See our separate CCT info sheet for details.

**Potential side effects and risks:**

Women on clomiphene may experience some hot flashes while taking it, because of its anti-estrogen effect.

Occasionally there may be some pelvic discomfort towards the end of the cycle, if there has been an exuberant response and good follicle development.

Cervical mucus may improve as the cycle improves and estrogen levels elevate, or it may paradoxically decrease, interfering with the ability of sperm to get into the uterus and tubes. Decrease in cervical mucus production can happen because clomiphene can fool the cervix, in addition to the pituitary gland, into thinking that estrogen levels are low. Women over age 30 more often have cervical mucus decrease with clomiphene, and thus we may recommend IUI (intrauterine insemination) to bypass the mucus in these women. (Please see our info sheet on IUI).

Sometimes, clomiphene will also fool the uterine lining into thinking that estrogen levels are too low, and this can result in the lining being too thin to let fertilized eggs implant. This can be measured using ultrasound.

Twins can occur in 3-5% of clomid conceptions. Multiples higher than 2 generally don't happen with clomiphene conceptions.

Small cysts on the ovary from too many follicles can sometimes occur. Occasionally a cyst develops that necessitates a rest cycle or a lower dose in a future cycle.

Although ovarian cancer has been found to develop more often in fertility patients, it is NOT associated with the use of fertility drugs. Rather the risk appears to be from never conceiving.