

Ovulation Induction with Clomphene



OVULATION

A common cause of infertility is due to a woman not releasing an egg (called anovulation). Normally, a woman's ovaries produce one egg every 24 to 35 days. Ovulation usually occurs about 14 days before the next menstrual period, under the control of two hormones released by the pituitary gland (LH and FSH). The best chance for becoming pregnant occurs around the day of ovulation. This would be approximately 14 days after the first day of a 28 day menstrual cycle (day 1 of the menstrual cycle is the first day of bleeding).

There are a number of different reasons why a woman may not ovulate, including polycystic ovarian syndrome (PCOS), premature menopause and low body weight. In some cases no specific cause is identified. There are different treatments recommended, depending on the cause. Women with PCOS are likely to respond to treatment with a drug called clomiphene. Women with very low oestrogen levels due to low body weight or exercise and those with high FSH levels, indicating premature ovarian failure are unlikely to respond to clomiphene and so other treatments may be recommended

WHAT IS CLOMIPHENE?

Clomiphene is a weak oestrogen-like hormone that acts on the hypothalamus, pituitary gland, and ovary to increase levels of FSH and LH. An increased level of these hormones increases the chance of growing an ovarian follicle that can then trigger ovulation. In women who ovulate irregularly, approximately 80 percent who take clomiphene will ovulate, and 40 to 50 percent of all women who take clomiphene for up to 3 cycles will become pregnant.

Pretreatment evaluation — Before any infertility treatment begins, a woman and her partner should undergo an infertility evaluation to be sure that clomiphene is the best treatment. This evaluation may include a complete history and physical examination, a semen analysis (for men), blood testing, ultrasound scan (for women) and other tests depending upon the individual situation.

Dosing — Clomiphene is usually started on day three of the menstrual cycle at a dose of 50 mg (one pill) once daily for five days. The first day of bleeding is called cycle day one. If the woman does not have regular menstrual cycles, after performing a urinary pregnancy test, she will be given a 5 day course of progesterone drugs treatment to induce a period.

Ovulation usually occurs between cycle day 14 and 19. In order to ensure that a woman is not releasing more than 2 eggs at once, we recommend ultrasound monitoring for women undergoing clomiphene treatment for the first cycle. This involves inserting a thin probe into the vagina and using sound waves to view the size and number of developing follicles (which contain an egg). The woman is advised to contact DFA to arrange a scan when starting treatment with clomiphene to arrange a scan around day 10 of her first cycle of treatment. If the scan shows one or 2 follicles are developing, the couple are advised to have intercourse every other day for the following week. Ovulation can then be checked by having a blood test arranged around day 21 of the first cycle.

If ovulation does not occur during the first month, the clomiphene dose is increased by 50 mg each month until ovulation occurs. An ultrasound scan and blood test will be arranged to check for ovulation. There is no benefit of increasing the clomiphene dose if ovulation occurs, even if pregnancy does not occur. Nearly all pregnancies occur within the first six ovulatory cycles while using clomiphene, and there is little benefit of continuing clomiphene treatment after six unsuccessful ovulatory cycles. If this occurs it would suggest the need to consider other infertility investigations, such as hysterosalpingogram or laparoscopy. Alternative treatments may then be considered, including gonadotrophin ovulation induction or IVF treatment.

Benefits — The benefit of clomiphene is that it is relatively inexpensive and can be used before other, more invasive testing or infertility treatments. Clomiphene improves the chances of becoming pregnant for most women who ovulate irregularly, and it carries a low risk of dangerous side effects.

Risks — Risks of clomiphene treatment include an increased rate of multiple pregnancies; approximately 10 percent of women who use clomiphene have twins, while less than 0.5 percent have triplets or greater. There is a small risk of the ovaries becoming enlarged, although severe enlargement (known as ovarian hyperstimulation syndrome) is rare.

Common side effects of clomiphene include hot flashes, headaches, abdominal bloating and pain, nausea and vomiting, mood changes, and breast tenderness. Visual symptoms such as blurring, double vision, or seeing spots occur in 1 percent of women, and are an indication to stop treatment.

Most studies do not show an increased risk of birth defects, miscarriage, or learning disability in children of women who took clomiphene. There is no increased risk of breast cancer or uterine cancer. There may be a slightly increased risk of ovarian cancer if more than 12 cycles of clomiphene are used.

IMPROVING CLOMIPHENE SUCCESS

Women who do not become pregnant after three cycles of clomiphene are usually encouraged to have further testing before continuing with infertility treatment. This may include a hysterosalpingogram (an X-ray test showing the uterus and fallopian tubes) or a laparoscopy (an operation involving key hole surgery to look at the uterus, tubes and ovaries). These tests can be arranged through DFA and are performed at Fernbrae Hospital. If these tests are normal and the couple would like to continue with clomiphene treatment, other interventions, such as weight loss or gain, might be suggested.

Weight loss — Women who are overweight or obese and who ovulate infrequently may benefit from weight loss as a treatment for their infertility. Overweight is defined as having a body mass index (BMI) greater than 25 kg/m². Weight loss is an inexpensive and low-risk treatment with no side effects that has been proven to improve the chances of ovulation and pregnancy in women who are overweight. It also reduces the risk of complications during pregnancy and has lifelong health benefits. A combination of decreased calorie intake and exercise are recommended to achieve weight loss.

Weight gain — Women who are underweight (defined as a BMI less than 17 kg/m²), have eating disorders (eg, bulimia or anorexia), or who participate in strenuous exercise regimens may not ovulate. These women may be advised to gain weight to a goal BMI of at least 19 kg/m² by increasing calorie intake, and modify exercise habits to include less strenuous activities.

Treatment with human chorionic gonadotropin — Some women do not have an increase in their LH level midcycle and do not ovulate, despite having a normally

developed follicle. These women often benefit from using an injection of human chorionic gonadotropin (hCG), which triggers ovulation.

Transvaginal ultrasound is used to assess when the follicle is ready, and the woman or her partner can be taught to give the injection at home. Ovulation occurs 36 to 44 hours after the injection, and intercourse can be timed. hCG may also be recommended for women who will have a procedure, such as intrauterine insemination.