

OVULATION INDUCTION

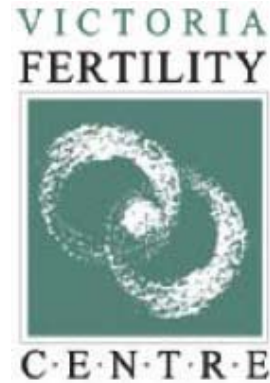
Before discussing ovulation induction agents (fertility drugs), I will briefly outline the physiology of the ovaries.

Unlike the testes in men, the ovaries are banks of eggs. In other words, a female is born with a finite number of eggs. It is interesting to note that when a female is a foetus, still in her mother's womb, she has around 5 million eggs. By the time she gets to her teenage years, she will have about 200,000 or 300,000 eggs left. In other words, there is a natural process by which eggs are dying all the time. Most women will start ovulating around the age of 13 years. Medically, this is called the menarche. Again, most females will ovulate once a month, meaning that they will release approximately 12 eggs per year. During a lifetime therefore, the eggs given up by the ovaries by ovulation amount only to about five hundred or so. This makes up a very small percentage of the eggs that are lost due to a natural aging process.

Most eggs are lying dormant (asleep) within the ovaries. At the beginning of each menstrual cycle the pituitary gland in the brain sends a message to the ovaries. This message is in the form of a hormone called FSH (follicle stimulating hormone). This hormone stimulates a certain number of eggs in the ovaries to start maturing. Each of these eggs starts growing in a tiny capsule of fluid called a follicle. For all intents and purposes these are cysts. The word "cyst", which often strikes fear into the hearts of most women, is just an adjective meaning fluid. It is normal for the ovaries to make little cysts (follicles) every month.

In any event, in response to the FSH from the brain a number of eggs start maturing in their little capsules of fluid which are called follicles. After two or three days one of these follicles (containing an egg) is selected to be the one that will ovulate. All the other little eggs which had started maturing will spontaneously regress. As this follicle grows the egg slowly starts maturing. The cells which line the inside of the follicle are called granulosa cells. As the follicle grows the granulosa cells produce estrogen, which reaches a peak at the same time that the egg reaches maturity. The brain, which is constantly monitoring the estrogen levels identifies when this threshold is reached as the time at which this egg is mature. The brain then sends a hormone called luteinizing hormone (LH) which tells the ovary to release the egg (ovulation). This is called the LH surge, which can be detected in urine using an ovulation predictor kit. Detecting this surge in the urine normally means that ovulation will occur the following day. Once ovulation has occurred, hopefully the egg is picked up by the fallopian tube, and will be exposed to fertilization by sperm which swim up from the vagina, through the cervix, into the uterus and along the tube.

After the follicle has released its egg its job is not done. It now forms a little cyst called a corpus luteum. This cyst starts producing a hormone called progesterone. Progesterone nurtures the lining of the uterus and makes it favourable for the embryo to implant. This progesterone also has a thermogenic effect so that a woman will notice that her temperature goes up slightly after ovulation. Unless pregnancy occurs, the cyst usually has a lifespan of only 14 days. After 14 days it dies, the progesterone level drops and menstruation occurs. The whole process then starts over again.



Fertility drugs come in various forms. They can be given either in pill form or as injections. The commonest pills used to induce ovulation are called Clomiphene, Letrozole or Tamoxifen. Clomiphene is by far the most commonly used.

The primary indication for using Clomiphene is in women who do not ovulate regularly on their own. Clomiphene is prescribed usually for five days, starting on either the third or fifth day of the menstrual cycle. In an indirect way it stimulates the pituitary gland to release more follicle stimulating hormone in the hope that this will result in recruitment of a follicle and ovulation. Letrozole and Tamoxifen work in similar ways. Clomiphene has common side effects – specifically, headaches, nausea, hot flashes, visual blurring and mood swings. Letrozole and Tamoxifen can also cause these side effects though are not quite as common.

These oral agents may also sometimes be used to enhance pregnancy in women who are ovulating regularly though not conceiving. However, their role in this particular regard is somewhat limited. They are also often used in conjunction with a treatment process called “ovulation induction with intrauterine insemination”. During this process the fertility drugs are given as prescribed, and the ovaries are monitored by ultrasound to identify how many follicles are recruited. When the follicles are mature another drug is given to trigger ovulation, and then a timed intrauterine insemination is performed either with donor sperm or washed sperm from the male partner.

The second group of fertility drugs are more powerful and are given by injection (because they are not absorbed by oral administration). The hormone FSH is available in two forms, manufactured by different companies, and known as either Gonal-F or Puregon. Another medication commonly used is a mixture of FSH and LH which is available in the form of a drug called Repronex. These drugs are given in various combinations and doses, by daily subcutaneous injections, usually starting on either Day 3 or Day 5 of your cycle. They are commonly used for in vitro fertilization as well. Rather than acting indirectly, these hormones directly stimulate the ovaries to mature many follicles. Whether being used for superovulation with intrauterine insemination or in vitro fertilization, the ovaries are closely monitored by serial ultrasounds and sometimes by measuring the estrogen levels in your blood.

The drugs themselves have very few side effects, although they can sometimes cause a local reaction where they are injected. The effects they do have are directly on the ovaries. With the ovaries making more follicles, they become larger in volume and can cause some pressure discomfort in the tummy. Secondly, they result in higher estrogen levels which can cause bloating, breast tenderness and sometimes nausea and other symptoms. The dosage of drug prescribed will always depend on the person’s age, weight and other clinical features such as ovarian volume on ultrasound. The main risks of using these drugs are either of multiple pregnancy or something called ovarian hyperstimulation syndrome. We use these drugs very cautiously, and it is uncommon to have serious side effects. Ovarian hyperstimulation, also abbreviated as OHSS, is more common during in vitro fertilization. Women who are most vulnerable for OHSS are women under the age of 35, and women with a history of PCOS. There is more information on OHSS under the section marked Downloads on this website.

The injectable fertility drugs are expensive – and obviously the final cost will depend on the dosage which is necessary to stimulate the ovaries.