Bourn Hall CLINIC

How do fertility drugs work?

Under normal circumstances, ovulation occurs once a month when a ripened egg which is ready to be fertilised is released from the ovaries. For couples who are trying to conceive, regular ovulation is incredibly important as this is when a woman is most fertile. If a woman isn't ovulating properly, fertility drugs can be prescribed in order to boost the natural system and increase the chances of successful conception.

Some fertility drugs can be prescribed by GPs and many couples are successful in getting pregnant with the help of these drugs alone. For example, Clomifene Citrate (often called Clomid) is a drug commonly prescribed to stimulate or regulate ovulation. It does this by blocking the receptors in the brain for oestrogen, which fools the body into thinking it is not making enough oestrogen. In response, the body increases production of follicle-stimulating hormone (FSH). FSH is key when it comes to fertility, as it allows a small group of follicles to grow and develop inside the ovary. Each of these follicles contains an egg, so by increasing the body's levels of FSH, the chance of the ovaries releasing a ripe egg for fertilisation is increased.

Other drugs prescribed by GPs included Metformin, which can be particularly useful for women who have polycystic ovarian syndrome (PCOS). Metformin is more commonly used as treatment for type II diabetes as it reduces levels of insulin in the blood. However, it has been found that for women with PCOS, metformin can also trigger ovulation.

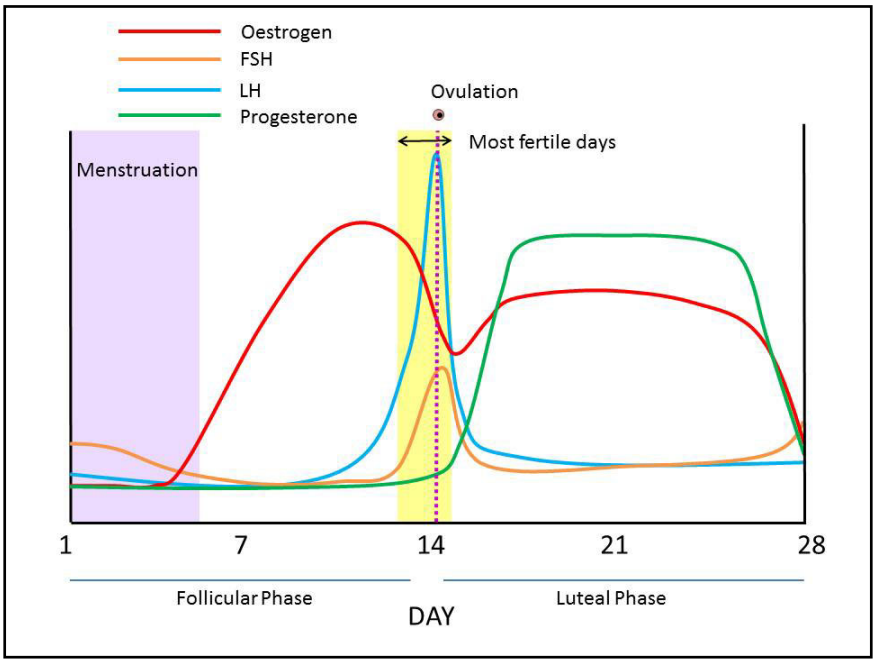
Fertility drugs and IVF

For those couples who are not successful in conceiving with the help of fertility drugs alone, treatments such as IVF may be recommended. During IVF, eggs are collected from the ovaries and fertilised outside of the body. After a few days of growth, embryologists very carefully select the embryo that they believe has the highest chance of success and this is transferred to the woman's womb.

Fertility drugs are essential during IVF treatment as multiple eggs must 'ripen' at precisely the same time so that they can be collected and fertilised. To do this, the natural fertility cycle is suppressed and then synthetic hormones are used to encourage the development of more than one egg.

Suppressing the natural cycle

During a natural cycle, it is the rise in luteinising hormone (LH) and follicle stimulating hormone (FSH) that triggers ovulation. The release of both LH and FSH is controlled by gonadotropin-releasing hormone (GnRH). When GnRH binds to its receptor in the brain, LH and FSH are produced by the pituitary gland and ovulation occurs shortly afterwards.



Hormone levels during the natural menstrual cycle: It is the rise in luteinising hormone (LH) and follicle stimulating hormone (FSH) that triggers ovulation around day 14.

In order to suppress natural ovulation, the receptors for GnRH must be switched off. If GnRH cannot bind to its receptors then LH and FSH will not be produced and ovulation will not occur.

Nafarelin and Buserelin acetate are two examples of ‘gonadotropin-releasing hormone agonists’. An agonist is a chemical that binds to a receptor and stimulates it, so both Nafarelin and Buserelin are capable of binding to GnRH receptors and causing the release of LH and FSH. You may think this is strange, as the idea is stop LH and FSH production, not stimulate it. However, once Nafarelin or Buserelin have bound to the GnRH receptors and caused an initial increase in FSH and LSH, the drugs then stay there and block the receptor from further stimulation.

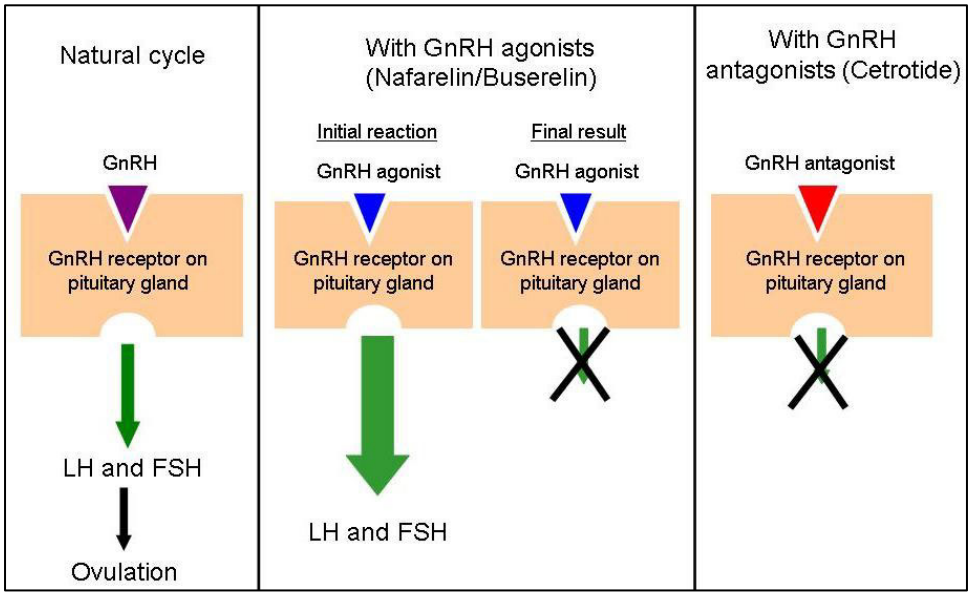
This means that after the initial increase in FSH and LH, the levels in the blood quickly drop and become very low. The levels will then stay low for as long as the woman takes the gonadotropin-releasing hormone agonists.

This is referred to as ‘pituitary down-regulation’, as the blocking of the GnRH receptors means LH and FSH are no longer produced by the pituitary gland.

As well as GnRH agonists, which first stimulate the GnRH receptor but then block it, other drugs called GnRH antagonists are also available.

GnRH antagonists work in exactly the same way as GnRH agonists to lower the natural levels of FSH and LH, however antagonists immediately block the GnRH receptors without stimulating them first.

One example of a GnRH antagonist that may be used in IVF is Cetrorelix acetate (Cetrotide). Although GnRH antagonists work faster than GnRH agonists in stopping production of FSH and LH, some patients may respond better to treatment with agonists.



Pituitary down-regulation: Drugs are used to prevent the natural release of FSH and LH.

Encouraging the development of multiple eggs (ovarian stimulation)

During a natural cycle, there is usually only one follicle each month that fully matures and releases an egg. For the egg collection process to be successful, multiple follicles must ripen and mature at exactly the same time.

Once the natural cycle has been suppressed, fertility drugs are given to encourage this ripening process.

FSH is crucial to the development of eggs and so a synthetic version of FSH such as Follitropin alfa (Gonal – F) is given via injection. In a natural menstrual cycle, FSH levels would begin to drop as follicles mature, so that only one (or occasionally two) eggs would be released for fertilisation. During IVF treatment, daily FSH injections mean that levels of the hormone are kept higher for longer so that multiple follicles are able to fully mature.

In addition to Follitropin alfa, Lutropin alfa is also given via injection. Lutropin alfa acts in the same way as luteinising hormone (LH) and helps to mature the eggs.

In a natural cycle, a sudden rise in LH is enough to trigger ovulation by itself, however during IVF, an additional injection of Choriogonadotropin alfa (often called Ovitrelle) is given around 36 to 40 hours before the egg collection procedure.

This injection is the final preparation before egg collection and ensures that several eggs are mature and ready to be fertilised.

Preparing the uterus for pregnancy

Once the egg retrieval process has taken place, the next stage is to prepare the uterus for implantation of an embryo. Progesterone therapy can be administered as a vaginal gel, intramuscular injection or capsule and is used in the majority of IVF cases to supplement the progesterone made naturally by the body. This is because during IVF treatment, a woman's ovaries may not be able to produce enough progesterone to thicken the uterine lining sufficiently.

During a natural menstrual cycle, the lining of the uterus (also called the endometrium) grows thick and rich with blood vessels and this is the optimum environment for implantation of an embryo. Progesterone supplementation at this stage of IVF treatment therefore ensures that the uterus is ready for pregnancy.

Taking fertility drugs

Individuals can vary in their response to fertility drugs, so the procedure is carefully monitored and the dosage is adjusted accordingly. Vaginal ultrasound scans are used to track development of the follicles during ovarian stimulation.

Fertility drugs can result in mood swings and other side effects. If you are concerned about how any of the medication is making you feel then do talk to one of the nurses or the pharmacist.

Fertility drug Summary

Drug Name	Brand Names	Details	Usage
Clomifene Citrate	Clomid	Clomifene Citrate can help stimulate ovulation in women who do not ovulate regularly.	Clomid is taken as a tablet.
Nafarelin acetate	Synarel	Nafarelin acetate is a GnRH agonist used to suppress the natural cycle. The chemical binds to GnRH receptors and stimulates them, causing an increase in levels of LH and FSH. However, after the initial increase, levels of FSH and LH drop and remain very low for as long as the woman continues to take the drug.	It is often administered as a nasal spray, designed to reach the blood stream quickly and efficiently.
Buserelin acetate	Suprecur	Buserelin acetate is a GnRH agonist used to suppress the natural cycle. The chemical binds to GnRH receptors and stimulates them, causing an increase in levels of LH and FSH. However, after the initial increase, levels of FSH and LH drop and remain very low for as long as the woman continues to take the drug.	It is often administered as an injection.
Cetrorelix acetate	Cetrotide	Cetrorelix acetate is a GnRH antagonist used to suppress the natural cycle. The chemical binds to GnRH receptors and blocks them, causing an almost immediate decline in FSH and LH levels. FSH and LH levels remain low for as long as the woman continues to take the drug.	Administered as an injection.
Follitropin alfa	Gonal-f	Follitropin alfa is a gonadotropin which acts in the same way as FSH. It is given in conjunction with Lutropin alfa to stimulate egg development in women.	It is administered by injection.
Lutropin alfa	Luveris	Lutropin alfa is a gonadotropin which acts in the same way as LH. It is given in conjunction with follitropin alfa to stimulate egg development in women.	It is administered by injection.
Choriogonadotropin alfa	Ovitrelle	Choriogonadotropin alfa is a synthetic version of human chorionic gonadotropin (HCG) – a natural sex hormone. It is used to stimulate the final maturation of eggs in the ovaries of women having IVF.	It is administered by injection.
Progesterone	Crinone	Progesterone is a naturally occurring hormone produced by the ovaries during the second half of the menstrual cycle. Progesterone is essential in the preparation of the uterus for pregnancy.	Crinone is administered as a vaginal gel; however progesterone therapy can also be administered via injection, capsule or suppository.