Infertility treatments (IVF)

Fertility treatment may be with medicines, with surgical operations, or by the use of assisted conception techniques, such as IVF.

Fertility treatments can be grouped into three categories:

- **Medicines to improve fertility** - these are sometimes used alone but can also be used in addition to assisted conception.
- **Surgical treatments** - these may be used when a cause of the infertility is found that may be helped by an operation.
- **Assisted conception** - this includes several techniques such as:
  - Intrauterine insemination (IUI).
  - In vitro fertilisation (IVF).
  - Gamete intrafallopian transfer (GIFT).
  - Intracytoplasmic sperm injection (ICSI).

Each of these is discussed briefly below.

Medicines that may improve fertility

Medicines are mainly used to help with ovulation. The process of ovulation is partly controlled by hormones called gonadotrophins. These are made in a gland just under the brain (the pituitary gland). A gonadotrophin is a hormone that stimulates the activity of the gonads (the ovaries in women and the testicles in men). The main gonadotrophins made by the pituitary gland are called follicle-stimulating hormone (FSH) and luteinising hormone (LH). These pass into the bloodstream and travel to the ovaries.

Clomifene

This is a medicine that has been used to help with fertility for many years. Clomifene is taken as a tablet. It works by blocking a feedback mechanism to the pituitary gland. This results in the pituitary gland making and releasing more gonadotrophin hormones than normal. The extra amount of gonadotrophin hormones may stimulate the ovaries to ovulate.

Clomifene has been tried for male infertility, and is used in some countries, such as the USA. However, there is little evidence that it actually helps men father a child, and so it isn't routinely used in the UK.

Medicines that contain gonadotrophins

Another type of treatment, these need to be injected. They are sometimes used when clomifene does not work. They may also be used prior to assisted conception techniques to trigger ovulation. Gonadotrophin medicines may be used in men who have a problem where the pituitary gland does not produce enough gonadotrophins normally (called 'hypogonadotrophic hypogonadism'), to improve their fertility.

Medicines that contain gonadotrophin-releasing hormone

These are sometimes used. These stimulate the pituitary gland to release gonadotrophins (which in turn stimulate the ovaries).

Metformin

This may be offered to women with polycystic ovary syndrome (PCOS) who have trouble conceiving. Metformin is a medicine that is commonly used to treat some people with diabetes. Some studies have suggested that metformin may help to improve fertility in some women with PCOS, usually in addition to clomifene.

Make sure you have a full discussion with your doctor before taking any medicine for infertility. This is so that you are aware of success rates, any potential side-effects or risks (see below) and also the latest research and evidence for these medicines.

Surgical fertility treatments

The situations where an operation may be an option include:

- **Fallopian tube problems** - surgery may help some women with infertility caused by Fallopian tube problems. These days, most surgery to the Fallopian tubes is done by keyhole surgery.
- Endometriosis. Surgery to remove areas of endometriosis can improve fertility for people with mild endometriosis. The evidence for surgery to improve fertility isn't as good in more severe cases of endometriosis, and surgery for severe endometriosis may involve more risks.
- **Polycystic ovary syndrome (PCOS)** - an operation on the ovaries may be suitable for some women with PCOS. The procedure is sometimes called ovarian drilling or ovarian diathermy. Again keyhole surgery is used. A heat source (diathermy) is usually used to destroy some of the tiny cysts (follicles) that develop in the ovaries. It may be done if other treatments for PCOS haven't worked.
- **Fibroids** - for women with fibroids, surgery (to remove the fibroid) may be considered if there is no other explanation for the infertility. The exact location of the fibroids also make a difference - fibroids that grow into the womb cavity ('submucosal fibroids') are more likely to cause fertility problems than fibroids in other places. However, small fibroids may not cause infertility.
- **Male infertility** - when there is a blockage in the tube inside the scrotum that is used to store sperm (epididymis), surgery may help. Some men have fertility problems due to a problem with veins in the testicle (a varicocele), and in some places operations to repair the varicocele are offered. However, the evidence shows that varicocele repair does **not** improve pregnancy rates, and so the UK's national guidelines say that this operation should not be carried out for infertility treatment.

Dr Krishna Vakharia, 16th October 2023
The National Institute for Health and Care Excellence (NICE) has recommended for those people specifically affected by treatment that could damage their ovaries and cause infertility, could be considered for surgery that removes and preserves their ovaries, and reimplant this tissue to offer a chance of becoming pregnant in the future. This is esepcially important to those that may have not reached puberty yet.
The evidence suggests that people who have had the procedure can become pregnant and have successful live births and it did not raise any major safety concerns.

Assisted conception

Current techniques are described briefly below. Your specialist will advise on which are options for your particular cause of infertility and will explain the chance of success. In the UK, the National Institute for Health and Care Excellence (NICE) has produced guidelines which explain the situations in which these techniques are available on the NHS.

Intrauterine insemination (IUI)

This is the process by which sperm are placed into the woman's womb (uterus). IUI is also suitable for single women or lesbian couples who want to get pregnant using donor sperm. It is done by using a fine plastic tube which is passed through the neck of the womb (the cervix) into the womb. Sperm are passed through the tube. It is a relatively straightforward procedure. It can be timed to coincide with ovulation (about halfway through a monthly cycle) in women who are still ovulating. Fertility medicines may also be given beforehand, to maximise the chance of ovulation occurring. Women who have this procedure need to have healthy Fallopian tubes to allow the egg to travel from the ovary into the womb. If successful, fertilisation takes place within the womb.

The sperm used can be either from a male partner, or from a donor:

- The male partner's sperm can be used when the cause of the infertility is unexplained and the sperm test results are normal. It may also be useful for cases where the female cervical mucus seems to block or kill the sperm. Sperm is obtained by the male partner masturbating just prior to the IUI procedure.
- Donor sperm are obtained from a sperm bank of frozen sperm provided by donors. It may be considered as an option in a number of circumstances - for example:
    - Where the male partner has no or very few sperm, or the sperm are not normal.
    - Where the male partner has had a sterilisation (vasectomy) but reversal has failed.
    - Where the male partner has an infectious disease such as HIV.
    - Where there is a high risk of transmitting a genetic disorder (a disease that is caused by an abnormality in either partner's DNA) to a baby.
    - If there is no male partner (for example, in a same-sex female relationship, or if a woman does not have a partner).

If IUI does not work, couples tend to move on to try other methods described below.

In vitro fertilisation (IVF)

IVF means fertilisation outside of the body. In vitro literally means 'in glass' (that is, in a laboratory dish or test tube). IVF is used in couples whose infertility is caused by blocked Fallopian tubes, or where their infertility is unexplained. It may also be used where there are certain problems with ovulation or a combination of factors causing infertility.

IVF involves taking fertility medicines to stimulate the ovaries to make more eggs than usual. When the eggs have formed, a small operation is needed to harvest them (egg retrieval). Each egg is mixed with sperm. This is obtained either by the male partner masturbating, or from a donor. The egg/sperm mixture is left for a few days in a laboratory dish. The aim is for sperm to fertilise the eggs to form embryos.

One or two embryos which have formed are then placed into the woman's womb using a fine plastic tube passed through the cervix. Any other embryos which have formed in the dish are either discarded or, if you wish, frozen for further attempts at IVF at a later date. You may also be asked to consider donating any spare embryos to be used for research, or to be donated to other infertile couples.

Around one in four IVF procedures result in a successful pregnancy. Your chance of success with IVF may be higher if:

- The female partner is under the age of 37.
- The female partner has been pregnant before.
- The female partner has a body mass index (BMI) between 19 and 30 (they are a good weight).

It is recommended that when IVF is used:

- Three cycles are offered to women aged under 40 years.
- One cycle is usually offered to women aged 40-42 years if they have not had IVF in the past.

The likelihood of IVF succeeding decreases after each unsuccessful cycle.

Gamete intrafallopian transfer (GIFT)

A gamete is an egg or sperm. Eggs and sperm are collected in the same way as for IVF. The eggs are mixed with sperm. The mixture of eggs and sperm is then placed into one of the woman's Fallopian tubes. Therefore, unlike IVF, the sperm fertilises the egg naturally inside the woman's Fallopian tube or womb, and not outside the body in a laboratory dish. GIFT is no longer recommended to be used instead of IVF.

Intracytoplasmic sperm injection (ICSI)

This technique involves an individual sperm being injected directly into an egg. (It is injected into the outer part of the egg - the cytoplasm.) This method bypasses any natural barriers that may have been preventing fertilisation. For example, some cases of infertility are due to the sperm of a male partner not being able to penetrate the outer part of the egg to fertilise the egg. ICSI can also be used when a male partner has a low sperm count, as only one sperm is needed.

If needed, a sperm can also be obtained by a small operation to the testicle (testis). This may be done when sperm cannot be produced in the usual way. For example, if the male partner has a blocked vas deferens, or has had a vasectomy.

The egg containing the sperm is then placed in the womb in the same way as with IVF. ICSI is used for couples who have failed to achieve fertilisation through IVF, or where the quality or number of sperm is too low for normal IVF to be likely to succeed.

Egg donation

This involves stimulating the ovaries of a female donor with fertility medicines, and collecting the eggs which form. The eggs are mixed with and fertilised by sperm of the recipient's partner (similar to IVF). After 2-3 days, embryos are placed in the womb of the recipient via the cervix. This method is an option in a number of circumstances - for example, it may be used:

- For women who have ovarian failure and cannot produce eggs.
- For women who have had their ovaries removed.
- For women who have conditions where the ovaries do not work (for example, in Turner syndrome).
- Where there is a high risk of transmitting a genetic disorder to the baby.
- In some cases of IVF failure.
- For same-sex male couples and single men wanting to become fathers (with a surrogate).

Embryo donation

Couples who have had successful IVF treatment may decide to donate any spare embryos to help other infertile couples.

Possible complications of infertility treatments

Multiple pregnancy

Twins and multiple pregnancy are more common in some forms of infertility treatment including medication treatment - for example, with clomifene. This is because in some of the treatments using medication, the ovaries may be stimulated so that more than one egg is released and therefore more than one egg may be fertilised. Also, in some assisted conception treatments, more than one embryo is put back into the woman's womb (uterus) and therefore more than one pregnancy can develop. This occurs less commonly now as latest guidelines advise that in most cases only one embryo be put into the womb.

Having twins or triplets may be a great thing for some couples. However, it should be explained that it does carry an increased risk of problems during a woman's pregnancy, such as high blood pressure and diabetes. There is also a higher risk of other complications such as a having a small baby or going into premature labour.

Pregnancy in the Fallopian tube

A pregnancy which develops in the Fallopian tube (an ectopic pregnancy) MAY be a little more likely in women who are undergoing treatment for infertility. This is especially if the cause of infertility is due to a problem with the Fallopian tubes. See the separate leaflet called Ectopic Pregnancy.

Stress

Going through investigations and treatment for infertility can be a very stressful thing and can put a strain on many relationships. It is important to discuss your feelings with your partner, doctor, nurse or counsellor.

Over-stimulation of the ovaries

There is a small risk that some of the medicines used to treat infertility, such as the gonadotrophin medicines, can over-stimulate the ovaries. This may lead to a condition known as ovarian hyperstimulation syndrome. In this condition, the ovaries can swell due to a number of cysts that develop on the ovaries.

Symptoms can include tummy (abdominal) pain and swelling (distension), feeling sick (nausea) and being sick (vomiting). The condition can usually be treated easily and does not lead to any major problems. However, occasionally it can be more serious and can lead to liver, kidney and breathing problems or a blood clot in an artery or vein (a thrombosis).

Close monitoring using ultrasound scans is often used when women are given medicines to stimulate the production of eggs by the ovaries. The numbers and size of the sac containing an egg (the follicle) can be measured. This helps to reduce the risk of multiple pregnancy and also ovarian hyperstimulation.

Other side-effects

Some of the medicines used to treat infertility - for example, the gonadotrophins - may cause hot flushes and menopause-type symptoms.

Before deciding to go ahead with any treatment, you should have a discussion with your infertility expert on the pros and cons of the treatment proposed and the risk of problems and side-effects.

Further reading

- Santos EP, Lopez-Costa S, Chenlo P, et al; Impact of spontaneous smoking cessation on sperm quality: case report. Andrologia. 2011 Dec;43(6):431-5. doi: 10.1111/j.1439-0272.2010.01089.x. Epub
- Fertility - Assessment and treatment for people with fertility problems; NICE Guidance (February 2013, updated September 2017)
- Balasch J, Gratacos E; Delayed childbearing: effects on fertility and the outcome of pregnancy. Curr Opin Obstet Gynecol. 2012 Jun;24(3):187-93. doi: 10.1097/GCO.0b013e3283517908.
- Manders M, McLindon L, Schulze B, et al; Timed intercourse for couples trying to conceive. Cochrane Database Syst Rev. 2015 Mar 17;3:CD011345. doi: 10.1002/14651858.CD011345.pub2.
- Learn about choosing a clinic; Human Fertilisation and Embryology Authority (HFEA)
- Our campaign to reduce multiple births; Human Fertilisation and Embryology Authority (HFEA)
- Infertility; NICE CKS, August 2018 (UK access only)

- Minhas S, Bettocchi C, Boeri L, et al; European Association of Urology Guidelines on Male Sexual and Reproductive Health: 2021 Update on Male Infertility. Eur Urol. 2021 Nov;80(5):603-620. doi: 10.1016/j.eururo.2021.08.014. Epub 2021 Sep 10.
- Fertility treatment 2019: trends and figures; Human Fertilisation and Embryology Authority (HFEA)
- Impact of COVID-19 on fertility treatment 2020; Human Fertilisation and Embryology Authority (HFEA)
- Bordewijk EM, Ng KYB, Rakic L, et al; Laparoscopic ovarian drilling for ovulation induction in women with anovulatory polycystic ovary syndrome. Cochrane Database Syst Rev. 2020 Feb 11;2(2):CD001122. doi: 10.1002/14651858.CD001122.pub5.
- Removal, preservation and reimplantation of ovarian tissue for restoring fertility after gonadotoxic treatment; Interventional procedures guidance, September 2023

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