

Infertility - a Summary of Treatments

This leaflet gives a brief overview of the main treatment options for infertility. Another leaflet called '*Infertility - a Basic Understanding*' gives some basic information on the causes of infertility and some general advice for couples trying to conceive. Further sources of detailed information are given at the end of this leaflet.

What are the main treatments used for infertility?

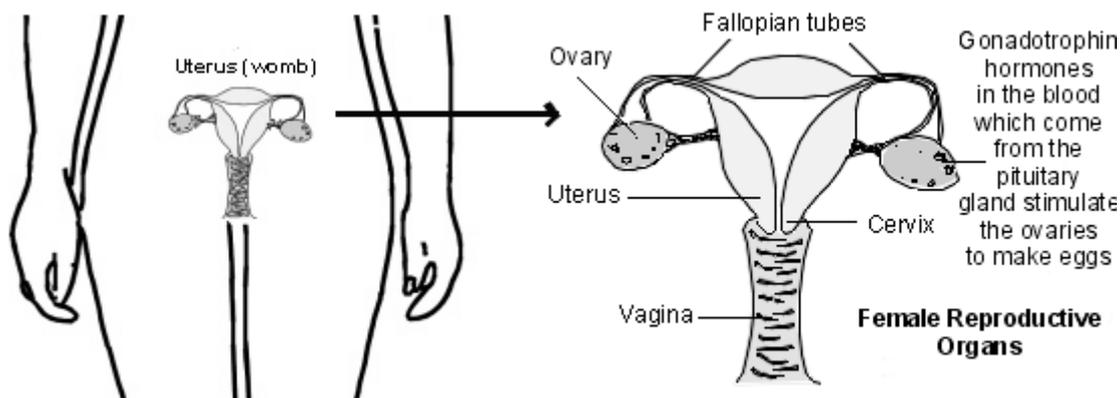
Fertility treatments can be grouped into three categories:

- **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), and intracytoplasmic sperm injection (ICSI).

Each of these is discussed briefly below.

Medicines (drugs) that may improve fertility

Medicines are mainly used to help with ovulation. Ovulation is when the ovary makes and releases an egg (ovum). Ovulation should occur about once a month in women up until the menopause. For various reasons, ovulation may not occur at all, or it may occur less often than normal.



Ovulation is partly controlled by hormones called gonadotrophins. These are made in the pituitary gland (a gland just under the brain). A gonadotrophin is a hormone that stimulates the activity of the gonads (the ovaries in women, and the testes 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** is a medicine that has been used to help with fertility for many years. It is taken as a tablet. It works by blocking a 'feedback' mechanism to the pituitary gland. This results in the pituitary making and releasing more gonadotrophin hormones than normal. The extra amount of gonadotrophin hormones released into the bloodstream stimulate the ovaries which may result in ovulation.
- **Medicines that contain gonadotrophins** are another type of treatment. These need to be injected and tend to be used when clomifene does not work, or prior to IUI and IVF to cause ovulation. Gonadotrophin medicines may also improve fertility in men

with certain types of hormone problems that can affect sperm count.

- **Medicines that contain gonadotrophin-releasing hormone** are sometimes used. These stimulate the pituitary to release gonadotrophins (which in turn stimulate the ovaries).
- **Metformin** may be offered to women with polycystic ovary syndrome who have infertility and who have not responded to clomifene. 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 polycystic ovary syndrome (PCOS), usually in addition to clomifene. However, another analysis published in the British Medical Journal recently suggested that the addition of metformin to clomifene has no significant benefit in improving fertility. So, at the moment, the role of metformin is a little unclear.

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 treatments

The situations where surgery may be an option include:

- **Fallopian tube problems** - Surgery to the fallopian tubes may help some women with infertility caused by fallopian tube problems. For example, if your fallopian tubes have been blocked or scarred from a previous disease, infection, or other problem. Some women who have had a 'tubal tie' (sterilisation) in the past for contraception may be able to have their fertility restored by tubal surgery. These days, most surgery to the fallopian tubes is done by 'keyhole' surgery.
- **Endometriosis** - Surgery may help to improve fertility in women with endometriosis.
- **Polycystic ovary syndrome** - A special operation on the ovaries may be suitable for some women with polycystic ovary syndrome. The procedure is sometimes called 'ovarian drilling' or 'ovarian diathermy'. Using keyhole surgery, a heat source (diathermy) is used to destroy some of the follicles (tiny cysts) that develop in the ovaries. It is usually done if other treatments for polycystic ovary syndrome haven't worked.
- **Fibroids** - For women with fibroids, sometimes surgery to remove the fibroid may be considered if there is no other explanation for the infertility. However, whether fibroids do cause infertility, and therefore whether they should be removed, is still uncertain.
- **A cause of male infertility** - One cause of infertility is due to sperm being blocked by an abnormality in the epididymis in the testis. This may be treated with surgery.

An operation used to be thought to help men who had a varicocele (like 'varicose veins of the testes') and who were infertile. However, a recent study has concluded that surgery is not likely to help in this situation. See separate leaflet called '*Varicocele*' for further details.

Assisted conception

Current techniques are described briefly below. Your specialist will advise on which techniques are options for your particular cause of infertility, and explain the chance of success.

Intrauterine insemination (IUI)

This is the process by which sperm is placed in the woman's uterus. It is done by using a fine plastic tube which is passed through the cervix into the uterus. Sperm are passed through the tube. It is a relatively straightforward procedure. It can be timed to coincide with ovulation (about half way through a monthly cycle) in women who are still ovulating. Fertility medicines may also be given beforehand, to maximize 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 uterus. If successful, fertilisation takes place within the uterus.

The sperm used can be either from the 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 seem fine, or for cases where the female cervical mucus seems to block or kill the sperm. Sperm is obtained by masturbation just prior to the IUI procedure.
- Donor sperm is obtained from a 'sperm bank' of frozen sperm provided by donors. It may be considered as an option when: the male partner has no or very few sperm; has had a vasectomy, and reversal has failed or not been tried; has an infectious disease such as HIV; there is a high risk of transmitting a genetic disorder to a baby.

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

In vitro fertilisation (IVF)

In vitro fertilisation means fertilisation outside of the body. In vitro literally means 'in glass' (that is, in a laboratory dish or test tube). IVF is mainly used in couples whose infertility is caused by blocked fallopian tubes, or unexplained 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 get them ('egg retrieval'). Each egg is mixed with sperm which is obtained in the same way as for IUI (described above). The egg/sperm mixture is left for a few days in a laboratory dish (often referred to as a 'test tube'). The aim is for sperm to fertilise the eggs to form embryos.

One or two embryos which have formed are then placed in the woman's uterus 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 (if the initial attempt fails to result in pregnancy). You may also be asked to consider donating any spare embryos to be used for research, or to be donated to other infertile couples.

Your chance of success with IVF may be higher if:

- The female partner is under the age of 39.
- The female partner has been pregnant before.
- The female partner has a Body Mass Index (BMI) between 19 and 30 (that is, they are not underweight or overweight).

Other things that may reduce the chance of success of IVF include:

- For the woman, drinking more than 1 unit of alcohol per day or consuming a lot of caffeine.
- For both partners, smoking.

It is recommended that couples should be given the chance of three complete cycles of IVF in order to have a realistic chance of conceiving. Most Primary Care Trusts in the UK currently offer one cycle of IVF on the NHS.

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 are 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 uterus, and not outside the body in a laboratory dish. For this to work, the woman's fallopian tube needs to be healthy. GIFT has been used in cases of 'unexplained fertility' or male factor infertility problems. However, it does not seem to be any more effective than IVF and so is not so commonly used.

Intracytoplasmic sperm injection (ICSI)

This technique involves an individual sperm being injected directly into an egg. (It is injected into the cytoplasm - the outer part of the egg.) 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 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 uterus 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 uterus of the recipient via the cervix. This method is an option for: women who have ovarian failure and cannot produce eggs; who have had their ovaries removed; who have conditions where the ovaries do not work (for example, Turner's syndrome); where there is a high risk of transmitting a genetic disorder to the baby. It is also used in certain cases of IVF failure.

Embryo donation

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

A note about treatment for unexplained infertility

Treatment for unexplained infertility tends to include either stimulation of ovulation using clomifene, intrauterine insemination or in vitro fertilisation. A recent study in Scotland looked at treatments for unexplained infertility including treatment with clomifene or treatment with intrauterine insemination. It compared these two treatments to no active treatment (that is, to couples just continuing to try to conceive naturally) over a six month period. The study found that those who were actively treated did not have any significantly higher pregnancy rates compared to those who just continued to try to conceive naturally. However, the women undergoing active treatment felt more reassured and found the process of treatment acceptable. The study did not look at the use of IVF as treatment for unexplained infertility.

This study raises the question about how to best manage unexplained infertility. The centre where you are being treated is likely to have their own protocols for treating couples with unexplained infertility depending on factors such as your age and your choices. You should discuss your options with the doctor who is treating you.

Other treatments

Some people suggest that supplements including zinc, selenium, and vitamin E supplements may be helpful for men who have abnormal sperm counts due to an unknown cause. However, the evidence to support the use of such supplements is a little weak.

Possible complications of infertility treatments

Multiple pregnancy

Twins and multiple pregnancy are more common in some forms of infertility treatment, including drug treatment, for example with clomifene. This is because in some of the drug treatments, 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 uterus and therefore more than one pregnancy can develop.

Having twins or triplets may be a great thing. 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 are also more likely to be complications for the developing babies as well such as a small baby, premature labour etc. For this reason, it is currently recommended in the UK that no more than two embryos are transferred during any one cycle of IVF for women under the age of 40.

Pregnancy in the fallopian tube

An ectopic pregnancy (a pregnancy that develops in the fallopian tube) is 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 separate leaflet called '*Ectopic Pregnancy*' for more detail.

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 drugs used to treat infertility such as the gonadotrophin drugs can 'over-stimulate' the ovaries and can 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 abdominal pain and distension (swelling), nausea and 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 thrombosis (a blood clot in an artery or vein).

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

Ovarian cancer

There has been some concern that some of the drugs used to stimulate the ovaries to ovulate may possibly increase the risk of cancer of the ovaries. Whether this actually is the case or not is uncertain. In fact, a recent large study in Denmark looked at women using fertility drugs (including gonadotrophins, clomifene and gonadotrophin releasing hormone) and found that they did not seem to increase the risk of ovarian cancer.

Birth defects

The overall risks of an abnormality (a birth defect) occurring following assisted conception is small. However, the risk is about 30% increased compared to babies conceived without assisted conception. A 30% increased risk sounds a lot. However, to put this in perspective in absolute numbers, around 3.5% of IVF babies have a birth defect compared to 2.5% of babies born without assisted conception. The birth defects found to be more common include certain heart problems, cleft lip and palate, and some abnormalities of the gut.

Other side effects

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

Before embarking on 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.

Ethical issues

Some infertility treatments are unacceptable to some people. This is mainly because of the wastage of embryos. For example, in IVF, embryos that are not used for implantation are discarded if they are not frozen for future use, donated or used for research.

Further information

This leaflet is a very basic overview of the treatments involved in infertility. Further sources of more detailed information include:

Infertility Network UK

Charter House, 43 St Leonards Road, Bexhill on Sea, East Sussex, TN40 1JA

Tel: 0800 008 7464 Web: www.infertilitynetworkuk.com

Provides advice and information for members of the public and for professionals on all aspects of infertility.

Human Fertilisation & Embryology Authority (HFEA)

21 Bloomsbury Street, London, WC1B 3HF

Tel: 020 7291 8200 Web: www.hfea.gov.uk

A statutory body which regulates, licenses and collects data on fertility treatments such as IVF and donor insemination, as well as human embryo research, in the UK. Has produced a comprehensive guide called 'HFEA Guide to Infertility' which can be downloaded from their site. The site also contains good information about [infertility treatments](#) such as [IVF](#).

Patient UK

The infertility section - www.patient.co.uk/showdoc/380/ - provides a large set of links to organisations and patient groups concerned with infertility and its treatment.

References

- [Fertility: assessment and treatment for people with fertility problems](#), NICE Clinical Guideline (2004)
- [Balen AH, Rutherford AJ](#); Management of infertility. *BMJ*. 2007 Sep 22;335(7620):608-11.
- [Bhattacharya S, Harrild K, Mollison J, et al](#); Clomifene citrate or unstimulated intrauterine insemination compared with expectant management for unexplained infertility: pragmatic randomised controlled trial. *BMJ*. 2008 Aug 7;337:a716. doi: 10.1136/bmj.a716. [abstract]
- [Balen AH, Rutherford AJ](#); Managing anovulatory infertility and polycystic ovary syndrome. *BMJ*. 2007 Sep 29;335(7621):663-6.
- [Donnez J, Jadoul P](#); What are the implications of myomas on fertility? A need for a debate? *Hum Reprod*. 2002 Jun;17(6):1424-30. [abstract]
- [Farquhar C](#); Do uterine fibroids cause infertility and should they be removed to increase fertility? *BMJ*. 2009 Jan 16;338:b126. doi: 10.1136/bmj.b126.
- [Jensen A, Sharif H, Frederiksen K, et al](#); Use of fertility drugs and risk of ovarian cancer: Danish Population Based Cohort Study. *BMJ*. 2009 Feb 5;338:b249. doi: 10.1136/bmj.b249. [abstract]
- [Reefhuis J, Honein MA, Schieve LA, et al](#); Assisted reproductive technology and major structural birth defects in the United States. *Hum Reprod*. 2009 Feb;24(2):360-6. Epub 2008 Nov 14. [abstract]

Comprehensive patient resources are available at www.patient.co.uk

Disclaimer: This article is for information only and should not be used for the diagnosis or treatment of medical conditions. EMIS has used all reasonable care in compiling the information but make no warranty as to its accuracy. Consult a doctor or other health care professional for diagnosis and treatment of medical conditions. For details see our [conditions](#).
© EMIS 2009 Reviewed: 13 Mar 2009 DocID: 4890 Version: 39