

Treatment Options

Ovulation Induction

The best method of stimulating the ovary will be decided according to individual needs. It can be achieved with mild stimulation using Clomiphene (Clomid) which is monitored by transvaginal scan (TVS). Gonadotrophin injections may be required as it has the advantage of being able to deliver longer stimulation cycles as required by its direct effect on the ovaries.

Intra-uterine Insemination (IUI)

Intra-uterine insemination is a relatively straightforward technique involving the insemination of a prepared sperm sample directly into the uterus at the time of ovulation. It can be done on an unstimulated cycles i.e. using naturally growing egg, in cases of unexplained infertility, but usually ovaries are stimulated either with Clomiphene or Gonadotrophin injections.

In addition to its role in unexplained infertility, IUI can be successfully used in cases of mild male problem such as a low sperm count and /or slightly weak sperm movement. Gonadotrophin stimulated IUI cycles are recommended in cases of endometriosis when the fallopian tubes are open.

What does treatment involve?

The insemination procedure involves depositing sperm directly into the uterus using a fine catheter which is inserted through the cervix via the vagina. As the timing of the insemination is crucial, the woman's cycle is monitored using ultrasound scans to assess the development of the follicles (the sacs in which the eggs grow) and occasionally urine tests to check for the time of ovulation. The sperm is inseminated when these tests indicate that ovulation is imminent.

In cases when it is appropriate to combine intra-uterine insemination with ovarian stimulation, the ovaries may produce more than one egg.

The partner is required to attend the clinic on the day of the insemination and produce a semen sample which is prepared in the laboratory to extract the most motile sperm. A pregnancy test should be performed two weeks after the inseminations.

In Vitro Fertilisation (IVF)

IVF is a technique involving the fertilisation of eggs by sperm outside the body. The term literally means 'fertilization in glass' - hence the commonly-used description 'test-tube baby' technique.

When is IVF Appropriate?

IVF was developed as a treatment for women who have blocked or badly damaged Fallopian tubes which prevent the egg and sperm from meeting. However, it may also be used in some cases where a woman has endometriosis, the male partner has poor quality sperm or where the cause of infertility is unexplained if other treatment measures fail.

What does treatment involve?

IVF treatment is made up of a number of procedures usually referred to as a 'treatment cycle'. An outline of what is involved in a typical IVF treatment is described below.

- **Down regulation** - Firstly, the woman is prescribed a drug taken in the form of a nasal spray or an injection which suppresses the release of the hormones responsible for the production of an egg. This is necessary in order to establish a 'baseline' from which to start ovarian stimulation and to prevent spontaneous ovulation before egg collection can take place.
- **Ovarian stimulation** - Once a base line has been established, the woman commences ovarian stimulation which takes the form of a daily sub-cutaneous injection. Stimulating the ovaries in this way should produce several eggs to ensure that there are enough suitable eggs for fertilization.
- **Monitoring** - Regular monitoring of the effects of the drugs on the ovaries is undertaken through ultrasound scans and blood tests.
- **Final injection** - When the ultrasound scan and blood tests indicate that there are a sufficient number of mature follicles (the sacs in which the eggs grow), a final injection is administered to ensure the ripening of the eggs in preparation for the egg collection.
- **Egg collection** - Eggs are collected from the ovaries through the vagina using a fine needle under ultrasound guidance to aspirate the eggs from the follicles. This is performed as a day-case in the Day Care Unit in the Bridge centre, typically under sedation.
- **Sperm production and preparation** - On the day of the egg collection, the male partner is required to produce a semen sample at the centre. The sample is then prepared in the laboratory to extract the most motile sperm.
- **Embryology** - When all the eggs have been collected, they are put in a dish with the prepared sperm and incubated in the laboratory. Approximately sixteen hours later, the embryologist will check to see whether fertilization has occurred.
- **Embryo transfer** - If fertilisation has occurred, usually two of the embryos are transferred directly into the uterus three to five days after the egg collection. The embryos are transfer through the vagina and cervix using a fine catheter. This procedure is usually pain free.

- **Pregnancy test** - A pregnancy test should be carried out fourteen days after the embryo transfer. If the result is positive, an ultrasound scan is recommended two or three weeks later to check the number of embryos, that the embryo is alive and situated in the uterus.

What causes IVF to fail?

During an IVF treatment cycle, a number of problems may arise which cause the treatment to be cancelled or to fail. These include the following:

- The ovaries may either fail to respond to the stimulating drugs or over-respond. In the former case the egg collection would not go ahead. In the latter case, it is Bridge policy to continue with down regulation but we hold the stimulating injection until it is safe to do the egg collection without risk of ovarian hyperstimulation.
- Very rarely, although ultrasound scans indicated the presence of follicles, no eggs will be found during the egg collection procedure.
- The collected eggs may fail to fertilise in the laboratory and therefore no embryos would be available for transfer.
- The eggs may fail to divide after fertilisation and therefore cannot be replaced into the uterus.
- After the embryo transfer, the embryos may fail to develop in the uterus. This is the most common reason for an IVF treatment not to result in pregnancy

Freezing and storage of embryos

In cases where more than three embryos result from an IVF treatment, it is sometimes possible to freeze and store these embryos - for five years in the first instance. This enables women to have a further treatment without the need for ovarian stimulation or egg collection.

In order to prepare the uterus to receive embryos, a course of drugs is administered to thicken the endometrium (the lining of the uterus). Embryos are then thawed (Defrosted) and replaced directly into the uterus. However, some embryos may deteriorate during the thawing process and would therefore not be replaced.

Intra-cytoplasmic Sperm Injection (ICSI)

The microsurgical fertilisation technique of ICSI is currently the most advanced technique available for the treatment of male infertility. It is used in conjunction with IVF and involves an extremely precise microscopic surgical procedure on an egg to assist fertilisation when each mature egg will be injected with one viable sperm.

When should ICSI be used?

ICSI can be used in cases where the man produced only a very small number of sperm which are incapable of penetrating the barriers surrounding the egg unassisted or the sperms motility is very slow. ICSI is also mandatory when sperm is directly retrieved from the testes. It can also be recommended in cases when fertilisation failed previously in an IVF cycle in spite of good sperm parameters.

What does the treatment involve?

Eggs and sperm are collected in the same way as in a normal IVF treatment. However, unlike conventional IVF, a single sperm is picked up from a prepared sperm sample in a very fine glass

needle and injected through the zona pellucida and the egg membrane directly into the centre of the egg. In this way, the sperm is not required to penetrate any of the surrounding barriers. The injected eggs are then incubated for sixteen hours and checked to see if fertilization has occurred. If fertilization does occur, up to two embryos are replaced 3 - 5 days after the egg collection as in a normal IVF treatment.

Treatment Options for male partners to retrieve Sperms

Microepididymal Sperm Aspiration (MESA), Percutaneous Epididymal Sperm Aspiration - PESA , Testicular Sperm Extraction - TESE

The total absence of sperm in the ejaculate is known as azoospermia. There are two main reasons for this occurrence:

1. A blockage or congenital abnormality, which prevents movement of the sperm between the testis (where sperm is produced) and the penis.
 - Blockage can be the result of previous vasectomy or previous infection.
 - Congenital abnormality presents as an absence of the tubes which carry the sperm from the testis to the penis. Some men are born with this 'congenital absence of the vas'. This condition is likely to be associated with an abnormal gene for Cystic Fibrosis.
2. A poorly functioning testis, resulting in low sperm production.
 - This may happen when the testis has been affected by conditions such as mumps, infections, trauma, testicular torsion or undescended testis, OR
 - Genetic abnormalities may be the cause. It is now recognised that up to 15% of men with azoospermia may carry abnormal genes responsible for their infertility. It is therefore important to perform a genetic screen to check this, not only to understand the problem, but also to assess the risk of transmission to the child.

However, in many cases, the reason for azoospermia will remain unknown.

In cases of testicular failure, it is now possible in around 50% of cases to collect at least a few sperm by performing one or multiple testicular biopsies. Provided some motile sperm are recovered, the chance of fertilization of the egg is again extremely good.

Techniques for Sperm Recovery

In the first instance, it is quite easy to recover sperm directly from either the testis itself or from the epididymis, which is like a small reservoir appended to the testis. However, the sperm that is collected is not able to fertilise the egg in the natural way and ICSI is always necessary. This leads to a fertilisation rate of around 65%. In most cases the procedure will be performed in the Day Case Unit (DCU) in the bridge Centre. You will be admitted one hour prior to the operation and will be discharged two to three hours later.

MESA

Sperm can be recovered either by open surgery needle or aspiration. During Microepididymal Sperm Aspiration (MESA) - the scrotum is opened and under microscope sperm is aspirated from the epididymis.

PESA

- The technique called Percutaneous Epididymal Sperm Aspiration, or PESA, is generally used where there is a blockage.
- Under local anaesthetic, sperm is aspirated directly from the epididymis, (tube containing the sperm), with a very fine needle which has been inserted through the scrotal skin.

An embryologist will then check the sample for the presence of sperm, under a microscope.

TESE

- The technique called Testicular Sperm Extraction, or TESE, is used in cases of non-obstructive azoospermia, or if PESA has been unsuccessful.
- This technique involves the collection of sperm directly from the testis.
- The patient may require an additional injection of intravenous drugs, to achieve a mild degree of sedation.
- A special needle, which allows the surgeon to recover several samples of testicular tissue from different locations, is used.
- A sample from the testicular biopsy will be sent for Histological examination in order to obtain a tissue diagnosis and also to rule out the risk of Testicular Cancer, which is known to occur slightly more frequently (1%) in men with non-obstructive azoospermia.

In both circumstances, it might be possible to freeze some sperm at the time of this operation so that it can be used during subsequent IVF/ICSI cycles, if the first one was unsuccessful.

Testicular Biopsy involves taking one or several small samples of the testes - either for analysis, or for the recovery of sperm in the most severe cases of azoospermia. These operations are done as day cases under general or local anaesthesia with or without intravenous sedation.

After the Procedures?

Patients are generally informed on the same day whether sperm has been found or not. However, in the most difficult cases, a two to three day period of tissue incubation is necessary before sperm can be recovered. Recovered sperm will be frozen for later use. There are generally enough sperm to perform several IVF / ICSI cycles.

The chance of recovering sperm is almost 100% if there is a simple blockage. With abnormalities of the testes, the average recovery rate is around 50% - 60%.

It is therefore important to understand that there is no guarantee of finding sperm even when the pre-operative tests seem encouraging.

Immediate Post Procedure Symptoms?

- You will start to feel some discomfort when the local anaesthetic wears off, a couple of hours after the end of the procedure.
- You will be given a prescription for antibiotics and painkillers.
- After a PESA, men are generally able to resume work a couple of days later. Convalescence takes 4-5 days after a TESE.
- In our experience complications are rare. Whilst some bruising or swelling can occur this rarely requires additional treatment, although post operative haematoma (a mass of clotted blood in the tissue) has been described in other literature. Furthermore, two cases of post-operative testicular atrophy have been reported worldwide.

IVF treatment following PESA / TESE?

Sperm extracted surgically is not able to fertilise eggs by routine IVF, so Intra Cytoplasmic Sperm Injection, or ICSI, is essential.

Fertilisation rates are 50-60% and the chance of pregnancy mainly related to the woman's age, with an average of 25- 35% per cycle.

Long Term Sperm Cryopreservation

Men may wish to have their sperm cryopreserved and stored in some circumstance:-

- Prior to undergoing Vasectomy.
- Prior to the treatment of some cancer which may involve the removal of a testicle or treatment such as chemotherapy or radiotherapy which may render them infertile.

Their sperm can be stored for a long period of time and used later on for infertility treatment such as insemination of their partner or IVF.

Vasectomy and Vasectomy Reversal

An increasing number of men have requested vasectomies over the last 20 years as it is a simple and reliable method of achieving male sterility.

Unfortunately approximately 3% of men regret their decision and request vasectomy reversal. These requests are more common if the vasectomy has been carried out at a time of personal or emotional crisis or following divorce.

It is important that vasectomy should not be considered a readily reversible method of birth control, however, as even in the best hands pregnancy rates are less than 50%. Because of this pre-vasectomy patients may consider freezing and banking of semen prior to their operation. This service is offered in centres licensed by the Human Fertilisation and Embryology Authority.

Before a Vasectomy

The sperm produced by each testicle collects in a tightly coiled tube called the epididymis. It is during their passage through the epididymis that the sperm achieve their ability to move and fertilise an egg. The epididymis leads into a thicker tube, the vas deferens. This can be felt in the scrotum of most men. The tube passes through the seminiferous vesicles and the prostate gland before leading into the urethra (the tube within the penis). It takes approximately 60 days for a sperm to be produced and a further 14 days to pass through the epididymis and vas deferens.

Vasectomy Reversal

Regret about vasectomy may be more common than suggested by the number of men requesting reversal (many couples request donor insemination rather than reconstructive surgery). Prior to vasectomy reversal the surgeon may suggest screening for antibodies. Achieving a pregnancy may be difficult if high levels are detected.

The operation may be performed using macroscopic, microsurgical or laser assisted techniques. Most operations require a general anaesthetic, although uncomplicated procedures are sometimes performed under local anaesthetic or epidural. The operation can take up to three hours, but can usually be performed as a day case procedure. However 7-10 days convalescence is required post operatively to assist the healing process.

An incision across the scrotum is required to expose the cut ends of the vas deferens. At this time it is important to ensure that sperm are present in the fluid that leaks out of the end of the

vas. If this is not the case there maybe a co-existing blockage in the epididymis and the operative procedure is then more complicated. The surgeon performing the operation may choose to reverse one side at a time. This allows the opportunity for repeat surgery on the other side if the first reversal is unsuccessful. Repeat reversal attempts on the same side however have a very low chance of success.

Methods of Vasectomy Reversal

i. Vasovasostomy

Here the cut ends of the vas deferens are opposed and sutured together. Patency of the vas deferens can be achieved in 80% - 90% of cases. However, only 30 - 40% of patients achieve a pregnancy following vasectomy reversal.

ii. Vaso-epididymostomy

Here the cut end of the vas deferens is joined to a tubule within the epididymis. Results achieved by this method are less good than with vasovasostomy.

Reasons for poor results:

- More than 10 years between vasectomy and reversal carries a poor prognosis
- Too much vas deferens removed at the time of the original operation
- The presence of high levels of anti-sperm antibodies
- Very rarely the testes may atrophy due to damage to the blood supply at the time of operation
- Age of the female partner > 35

Difference between patency and pregnancy rates.

Not every couple will achieve a pregnancy even if sperm appear in the ejaculate following reversal. Gradual scar tissue formation may cause stricture and finally re-blockage of the vas. In addition the semen quality after vasectomy reversal may be poor and IVF/ICSI may still be necessary to achieve a pregnancy. Anti-sperm antibodies may appear in the ejaculate after vasectomy reversal. These attach to the sperm and decrease their fertilising capabilities.

Treatment of anti-sperm antibodies.

- "Washing" the sperm sample has not proved to be very successful as antibodies are tightly bound to the sperm.
- Steroid tablets may help but have major side-effects if used in high doses.
- In vitro fertilisation (IVF) may be suitable for some cases. If spontaneous conception fails to occur - this may be a good option in order to test the fertilising capabilities of the sperm. If the sperm are unable to fertilise the egg in the normal way intracytoplasmic sperm injection (ICSI) is indicated.

Follow-up after Reversal

Sperm may appear in the ejaculate up to a year after vasectomy reversal. If this does not occur, further investigation is indicated. The female partner should already have been fully investigated. For the male partner - testicular biopsy should be considered prior to further surgery to ensure that the testes are still functioning normally.

Percutaneous Epididymal Sperm Aspiration (PESA)

If reversal has failed, sperm may be retrieved surgically from the epididymis and used for

IVF/ICSI. The retrieved sperm is fragile with low motility and usually has to be injected into the egg in order to achieve fertilisation. Occasionally reconstructive surgery can be performed at the same time. PESA is indicated for patients with congenital absence of the vas or irreparable and bilateral damage to the vas or epididymis.

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