

A guide to In Vitro Fertilisation (IVF)



Introducing Fertility Plus

Fertility Plus is a leading fertility clinic based in Harley Street, dedicated to offering couples and individuals the best chance of conception in a supportive, caring and confidential environment. We believe your care is paramount and we ensure that each of our patients receive personalised care, meaning the same doctor every visit, with fixed pricing and no hidden costs.

What is IVF?

In vitro fertilisation (IVF) is a process by which an egg is fertilised by sperm outside the body. It literally means "fertilisation in glass". Once fertilised, the embryos are monitored and transferred back into the uterus at the correct time.

IVF & ICSI Treatment Stages

IVF treatment is divided into the following stages:

- · Investigation and assessment
- Ovarian stimulation
- Egg collection
- Fertilisation
- Embryology and embryo transfer

Assessment

The assessment is an initial series of tests that include a sperm count, ovarian reserve test, blood test and scan. Following the results of these tests an IVF treatment plan will be given alongside the consideration of the fertility drugs that will be used and the associated fixed price package. Please inform us of any medication you are taking and do not stop any medications without prior consultation. Folic acid should be commenced before the IVF procedure.

Treatment Protocols

Start of treatment is either planned with the period or with certain adjustments to the period with the addition of tablets which are called pre-treatments. A clear plan will be given that is tailored to the individual.

The protocols used are:

- 1. The antagonist protocol, which allows for a shorter cycle with the addition of a drug to block ovulation.
- 2. The long protocol is where the small central gland in the brain is desensitised and stimulation of the ovaries commence. This is used less frequently in our practice.

Fertility drugs

Drugs play a key role in ensuring the success of IVF, the main drugs that we use in our IVF cycles at Fertility Plus are:

- Gonadotropins (FSH/LH): these are known as stimulation injections as they stimulate the ovary and push the antral follicles to start growing. There are different preparations called Merinol, Gonal F and Fostimon, all of which contain approximately the same primary drug called follicle stimulating hormone (FSH).
- Antagonist (Cetrotide): this is a drug that is given to block ovulation. It is usually given from day 5,6 or 7 of stimulation or in some cases later. The success rate of this drug is approximately 99.5% with failure (early release of eggs) in very few cases.

3. Trigger injections (Gonasi /Ovitrelle/Suprecur): these are given to trigger the release of the egg to get the ovary ready for egg collection. This injection is always taken at night at a specific time The failure rate (where no eggs are obtained) of all triggers is approximately 2-3%.

Ovarian Stimulation

Once we have agreed your plan we will either commence treatment with the start of your period or after a short period of pre-treatment. Stimulation injections are self-administered, taken daily at approximately the same time and are usually required between 10-14 days. The injections are administered just under the skin, in the tummy or thigh. The response to the FSH injection is monitored through regular scans and blood tests.

During ovarian simulation Cetrotide (an antagonist) is given to block the LH surge and ovulation occurring prematurely. This is usually given day 5 or 6 of the ovarian stimulation cycle (FSH injections) and is continued until the day of the trigger.

During stimulation the follicles (fluid filled sacs) which may contain an egg, are scanned and their size is measured, an oestrogen blood test may also be performed. Depending on the progress of the follicles, the dose of the medication may be adjusted.

Can the size of the follicle or the oestrogen test indicate that the follicle may have an egg?

During ovarian stimulation many follicles may grow though some may not give an egg. Neither the scan nor oestrogen test can give an indication if there are eggs inside the follicles. Eggs can only be studied when a needle is inserted inside the follicle and the contents of the follicle are drained and examined.

How do the follicles grow?

The response of the follicles in the ovary differ from person to person. The aim of stimulation is to get a reasonable number of follicles growing in order to achieve a good egg count. The stimulation and treatment plan is made following a review of the results of all the tests taken in addition to any previous IVF cycles undertaken by the patient. Even on low or maximum doses the ovaries can sometimes fail to elicit the response we expect. Some ovaries with a good reserve may also give a relatively lower response and there is no way to know the quality or the quantity of the eggs in the follicles.

When are the eggs collected?

When the follicles are large enough, the egg collection procedure is planned. The egg collection injection (or trigger injection) is usually given 35-35½ hours before the egg collection process, therefore always done late at night. This has to be done at the most specific time and either of the two injections may be prescribed, or sometimes a combination of both. It is very important that the trigger injection be taken at the prescribed time.

Which triggers are used?

- 1. Suprecur is a hormone that makes your pituitary gland release the LH hormone, thus mimicking nature. This significantly reduces the risk of ovarian hyperstimulation syndrome, though when given on its own, freezing embryos may be preferred. The endometrium goes out of sync and is less receptive to the embryo trying to implant.
- 2. HCG injection is a pregnancy hormone which mimics the LH hormone. This is a more traditional trigger that has been used for many years, but it increases the risk of ovarian hyperstimulation syndrome. This injection must be taken at night.

Both triggers have to be taken at the specific time at night.

The triggers have a small failure rate of approximately 2-3.5% but unfortunately this can't be known until the egg collection procedure is completed.

Points to be noted during ovarian stimulation

- The hormones must be injected daily around the same time. This may continue from 10 to 11 through to 14 days.
- · Cetrotide may be started around day 5 or 6, usually in the morning.
- Use barrier contraception throughout the procedure to avoid the chance of a pregnancy.
- · If the period start is irregular a pregnancy test is advised.
- Ensure that you have at least 2-3 days of medications stock left.

The semen sample

If the male partner is involved, a semen sample which is used to fertilise the egg is usually collected on the same day. We will ask him to abstain from ejaculation for at least three days and not have a long period of abstinence. When very low sperm counts are obtained, the embryologist may ask for a repeat sample to be provided on the same day. The sperm is collected in a room and if the male partner feels that he cannot do the sample and needs to bring it from home it is important he lets the team know early and a sperm sample can be produced at home with prior consent and arrangement.

Egg Collection

Egg collection is where follicles in the ovary are aspirated and the eggs are obtained. It is a day case procedure performed at the London Women's Clinic in the morning.

You arrive at the London Women's Clinic, 113 Harley Street between 7.30-8am where you will be seen by the nurses followed by your consultant. The anaesthetist will reassess you, checking your name and date of birth along with the embryologist. This is also checked on the dishes by electronic witnessing which is carried out by the laboratory.

A small cannula will be placed on your hand and sedation is given through your vein. This is not a general anaesthetic hence the recovery is much quicker and you will not feel the procedure.

The procedure is performed trans-vaginally, a fine needle is attached to a scan probe which is passed through the ovary. The fluid in the follicle is aspirated and sent to the embryologist to be checked for an egg. If an egg is not found the follicle may be flushed with sterile fluid to see if that detaches the follicle. This process may be repeated a couple of times.

Every follicle may not contain an egg and the egg to follicle ratio, the number of eggs which may come from each follicle may vary. In some cases the follicles may not yield any eggs or may provide abnormal ones. After the egg collection we are told how many eggs are obtained. There is no way of predicting the number of eggs or their quality until the egg collection.

Important notes about egg collection:

- 8 hours of fasting, food and water, is required. We request nil by mouth from midnight.
- You may take a shower in the morning. Avoid wearing any make-up, nail varnish or jewellery and leave any valuables at home.
- It is essential that a friend or relative takes you home afterwards.
- You may feel drowsy on the day and we suggest that somebody is at home with you for 24 hours following the procedure.

Post egg collection

Serious complications are rare but it's important watch for signs of severe pain, bloated feelings and dizziness where you would need to contact the emergency number as soon as possible. You may have some vaginal discharge which will become lighter.

Progesterone may be prescribed starting from the day of the egg collection if a fresh transfer is planned, alternatively if a frozen transfer is planned we may restart the Cetrotide and a drug known as Cabergoline to reduce the chance of ovarian hyperstimulation syndrome.

Fertilisation

The eggs are fertilised by either IVF or ICSI and whichever fertilitsation process is performed the sperm is usually prepared before the fertilisation procedure.

With IVF, the sperm is washed and mixed with the eggs in a controlled environment. It then depends on nature to fertilise the eggs. Failure rates (fertilisation of none of the eggs) for fertilisation with IVF vary between 1-5%, when none of the eggs can be fertilised and need to be discarded.

ICSI involves selecting a single sperm by a senior embryologist and injecting into the egg under a high powered microscope. There is approximately a 1% chance of failure to fertilise eggs after ICSI treatment.

Eggs either come as mature, immature or germinal vesicle. Mature eggs have completed the segregation process where certain chromosomes are discarded, thus making them ready for fertilisation. Immature eggs have not had the segregation of chromosomes and have double the number of chromosomes and cannot be fertilised. Germinal vesicles have not yet gone through the process of egg formation and are discarded.

The mature and immature egg varies from patient to patient; with older women and women with polycystic ovaries there is a higher proportion of immature eggs. At ICSI treatment the cells around the eggs are removed to check for maturity. Immature eggs are not injected with sperm. ICSI usually fertilises more mature eggs than IVF.

The next morning a fertilisation check takes place, the embryologist looks at all the eggs that have been fertilised to see if embryo creation has started. Fertilised eggs are called embryos, and these start to divide over in the days following fertilisation. This division is morphologically seen by the embryologist as follows:

- Day 1: a single cell with two pro-nuclei
- Day 2: 2 to 4 cells
- Day 3: approximately 5 to 9 cells
- Day 4: collection of multiple cells called a morula, approximately 30 to 40 cells
- Day 5 to 6: this is blastocyst stage containing 100 to 150 cells which start with certain cells forming a complex cellular structure whilst getting ready for implantation

Not all embryos become blastocysts and significant number of embryos may not turn into blastocysts. Approximately 20-30% of all fertilised eggs convert to a blastocyst and this may vary with age (increasing age yields less blastocysts), egg reserve and the sperm quality. A blastocyst culture is planned if there are more than 3 good quality embryos on day 3. Sometimes we may not be able to achieve a blastocyst culture and embryos may need to be frozen or transferred at an earlier stage. It is important to realise that the assessment of embryos is based on morphology (how they look) and not genetic. Good quality does not confirm genetic normality and embryos can be abnormal from 40% (<30 years) to 80% (>40 years).

We monitor these cells, and the embryologist will plan the transfer or freezing of embryos either on day 3 or day 5.

IVF Complications

IVF has been carried out for almost 25-30 years and during this period the risks have decreased significantly. The risks of IVF are few but significant when they occur.

Multiple pregnancies and ectopic pregnancies

This seems to be the most common risk of IVF. Since the embryos are implanted, there is a higher proportion of multiple pregnancies with complications of pre-term labour and increased risk of miscarriage. More information can be obtained from the HFEA site: http://www.oneatatime.org.uk

There is also a higher chance of having an ectopic pregnancy, since the embryos which are deposited in the womb may tend to move into the tubes.

Ovarian hyperstimulation syndrome

This is one of the most serious complications of IVF and it increases when more than 10 to 15 follicles may be growing with high oestrogen levels. It tends to occur more commonly with polycystic ovaries and in some cases where the response is extremely high we may decide to abandon the cycle.

Fortunately, the use of the analogue trigger Suprecur almost eliminates any moderate or severe ovarian hyperstimulation syndrome, though in rare cases we may still see some moderate hyperstimulation syndrome. The symptoms include abdominal pain, swelling, vomiting and shortness of breath. Mild ovarian hyperstimulation syndrome tends to occur in cases of polycystic ovaries, although with the analogue trigger it may be milder. We give Cetrotide and Cabergoline to reduce the symptoms. In a small number of cases you may need to be admitted to hospital.

Pelvic infection

Pelvic infection is extremely rare and unlikely to occur unless there is very bad scarring in the pelvis due to past surgery. We always use clean aseptic techniques and prescribe antibiotics.

Injury to bowel, bladder and bleeding

These are extremely rare complications where either the bowel or bladder is punctured or very rarely there may be excessive bleeding. With punctures to ovaries some of these may bleed and may present as complications. In these occasions you would have extreme pain, shortness of breath, feeling feverish, nausea and may need to be admitted to A&E urgently.

Adverse effects, eggs and embryos

There is a possibility of some eggs not being mature enough or a large number of eggs being immature. There is a small risk of 1-5% of fertilisation not occurring in IVF cases and in less than 1% of ICSI cases. There is a small proportion of women who have a very poor response and risk of failure of fertilisation is much higher in those cases.

Adverse effects of medications

The FSH injections are Merional , Fostimon , Menopur, Gonal F and Cetrotide. The most common side effects are a local reaction, occasionally fever or flu-like symptoms, some amount of muscular skeletal pain and dizziness. You may feel very bloated and may have mood swing and hot flushes. In the case of an antagonist, there is likely to be more of a reaction at the injection site, whereas in the case of the long protocol there may be dizziness, a slight increase of blood pressure or vaginal dryness and hot flushes and mood swings.

The progesterone given after the embryo transfer tends to cause bloating and some women may not tolerate vaginal pessaries.

Embryo Transfer

Embryo transfer is performed either as a fresh cycle immediately after egg collection, depending on the progress, or as a frozen cycle. In a fresh cycle we assess the embryos depending on the number of cells and the grading, which depends on a small number of fragments which the embryos create whilst they are dividing. One or two of the best embryos are chosen, and they are transferred with the help of a very small catheter, using a technique similar to that of a cervical smear under ultrasound guidance.

Unless requested embryo transfers are not performed under sedation and this would incur an additional charge.

Important notes about embryo transfer

• Arrive at least 30 minutes before the embryo transfer and with a full bladder. We normally advise women to empty their bladders around two hours before the procedure, and then drink approximately 1-1½ litres of clear fluid.

- · Do not wear any perfume and ask your partner not to wear aftershave.
- · If sedation is planned, fasting is required so an IV line can be inserted.
- Once the procedure is completed you can go home and rest for the day. We do not advise long term rest as there is no evidence of improved chances of pregnancy. After an embryo transfer you can return to normal as the embryos are quite safe in the uterus.
- The embryologist will advise if any further embryos have been frozen.

Which embryos are frozen?

Embryos that reach blastocyst (day 5 or 6) stage are frozen. All embryos may not reach blastocyst stage and we may need to freeze embryos on day 3 if there are 3-4 embryos of good quality. Blastocysts survive the freeze and thaw process better than day 3 embryos.

How long can embryos be frozen?

Embryos can be frozen up to 10 years and in special circumstances frozen longer. The laboratory charges a yearly fee for storage which is paid directly to the London Women's clinic.

Pregnancy test

If a test is positive, we ask you to continue all the medications and arrange a scan in about 6 to 7 weeks' time. Inform us if there is any vaginal bleeding or discharge or any sign of pain. If a test is negative, stop taking the medication, unless you are on steroids, which need to be tapered off.

If you wish to see your consultant sooner, please let us know and if you feel you need to speak to a counsellor an appointment can be arranged.

Is the rate of miscarriage higher with IVF than normal conception?

The rate of miscarriage is not higher with IVF. The risk of miscarriage increases with age. IVF treatments may pick up more biochemical pregnancies since blood tests are done before the start of the period and some very early pregnancies may be detected.

Is the risk of ectopic pregnancy higher?

When replaced the embryos take around 4 to 6 days to start implanting. It is well known that some embryos may migrate into the tubes and implant in the fallopian tubes. It is very important to detect them and diagnose them early though it may not be possible at all times. The incidence of ectopic pregnancy in an IVF cycle is approximately 1%.



To book a consultation with Mr Amit Shah or Mr Anil Gudi to discuss your personal requirements, please contact:

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For further information please visit:

www.fertilityplus.org.uk