


In Vitro Fertilisation (IVF) & Intra-Cytoplasmic Sperm Injection (ICSI)



Leicester Fertility Centre
Caring at its best

Information for Patients and Partners



University Hospitals of Leicester 

NHS Trust

What is this leaflet about and who is it for?

This leaflet explains what is involved when undergoing In Vitro Fertilisation (IVF) or Intra-Cytoplasmic Sperm Injection (ICSI). The difference between IVF and ICSI is the way the sperm is used to fertilise the eggs.

Your consultant will inform you whether IVF or ICSI is the recommended treatment choice for you.

What is IVF?

IVF is the process of fertilising eggs outside of the body. The eggs and the sperm are mixed together in a dish and are incubated overnight to allow fertilisation to occur. In the event of the sperm quality being insufficient for IVF on the day of egg collection we will discuss the option of ICSI treatment with you.

The main indications for IVF are:

- Age >40 years or more and/or reduced ovarian reserve
- Blocked or damaged fallopian tubes
- Endometriosis
- Borderline sperm parameters
- Unsuccessful Intrauterine Insemination (IUI) treatment

What is ICSI?

ICSI refers to the technique of injecting a single sperm into the mature egg. This helps the sperm to fertilise an egg. Eggs are prepared for injection by removing the outer cells known as the cumulus. A high-powered microscope is used to assess egg maturity (not all eggs will be mature) and the mature eggs are carefully injected with a single sperm.

The main indications for ICSI are:

- Male factor subfertility
- Surgically retrieved sperm
- Failure to fertilise in a previous IVF cycle
- Low fertilisation observed in a previous IVF cycle.

What preparation is needed for IVF or ICSI?

Prior to starting your treatment:

- 1) We would recommend that your Body Mass Index (BMI) is between 19 and 30 to ensure the best response to your treatment. Your BMI is calculated by your body weight in kilograms divided by your height in metres squared. You can use the online NHS Choices BMI calculator to know your BMI. If your BMI is above or below these levels you can seek support via your GP.
- 2) An ovarian reserve blood test, known as Anti Mullerian Hormone (AMH), is required, which can be done on any day of the cycle.
- 3) Screening blood tests are required for Hepatitis B and C, HIV 1&2, HTLV 1&2 and Syphilis for individuals undergoing treatment, valid for up to 3 months before commencing treatment.
- 4) If you have a medical condition that has been identified as having an impact on your treatment or pregnancy, you might be referred for anaesthetic review and/or pre-conception counselling and/or other specialist review. Treatment will not be commenced until considered safe.

What is the procedure?

You will be provided with relevant written information about the treatment process to support your understanding of the consent forms. For further information about the consent forms please visit the Human Fertilisation and Embryology Authority (HFEA) website: <http://www.hfea.gov.uk>

You will then receive an appointment to discuss and plan your IVF/ICSI treatment.

Before starting the treatment cycle you will be required to complete the consent forms and given the opportunity to ask any questions. After this process is completed and you are ready to start your treatment cycle, on the first day of your proper flow of the period you will call the unit on 0116 258 5922 to book for an ultrasound scan (called as the

antral follicle count (AFC) scan). This is an internal scan (transvaginal) to count the antral follicles (2 - 6mm in size) on the ovaries, done once between days 2 - 6 of the menstrual cycle. This scan will help us to decide the type and dosage of drugs required for you.

If your AFC is less than 5 including both ovaries, then we will not be able to commence treatment. We will then ask you to call on the first day of your next menstrual cycle. This we can try maximum for three times. If we do not achieve the required count you will have a medical review.

If ready to proceed further, the nurses will then arrange for medication collection and a kit bag. An injection lesson will be arranged if necessary.

Ovarian Stimulation Regimes

Depending upon individual assessment, you will follow a long or short protocol.

Long downregulation protocol

This involves a daily injection of Buserelin (Suprecur) starting approximately one week before your period is due in order to switch off the pituitary gland which controls your ovaries. The injection is to be administered every morning at the same time before 9:00 am; you will then have a period in 7-14 days. On the first day of proper flow of this period you will call the unit on 0116 258 5922 to book for a **baseline ultrasound** scan and blood test. This is to check that you have responded to the Buserelin injections. If all is well, in addition to the morning injection, you will be commenced on another daily injection (gonadotrophins) in the evening to stimulate the ovaries. You will be issued with a written plan detailing when your blood test and scans take place over a two week period to check that your ovaries are responding. The dose of your drugs will be altered dependent on your response.

Short protocol

If your blood tests or AFC on your ultrasound scan predict that you are more likely to over respond to ovarian stimulation drugs you may require a short cycle. You will contact the nurses on day 1 of your period to organise a blood test and scan. You then commence your daily injection of Gonadotrophins. You will also be advised to commence daily Cetrotide or Ganirelix injection 5 - 6 days later. You will be issued with a written plan detailing when your blood test and scans take place over a two week period to check that your ovaries are responding. The dose of your drugs will be altered dependent on your response.

Patients are advised to avoid unprotected intercourse during treatment.

What happens next?

Once the ultrasound scan shows that there are a sufficient number of mature follicles, you will be instructed to give a hormone injection of hCG (Ovitrelle) which matures the eggs before they are collected.

35 – 37 hours after the hCG injection, the eggs will be removed from the ovaries. The eggs are collected by means of a fine needle being passed through the vaginal wall into the ovaries under ultrasound guidance. You will be given sedation anaesthesia and not feel or remember the procedure. The medications that we use for your sedation anaesthesia include: Propofol, Alfentanil, Midazolam; these medications make you drowsy and provide pain relief. Diclofenac suppository can also be given rectally to provide pain relief for up to 18 hours after your egg collection.

On the day of egg retrieval your partner will be required to produce a sperm sample at home. **We advise a sexual abstinence of 2 or 3 days prior to producing a sperm sample.** Our embryology team will prepare this so that the best sperm are isolated and used to inseminate your eggs.

Blastocyst Culture

Blastocyst or extended culture is the term used when the embryos are cultured for five days following the egg collection. The embryo at this stage of development is known as a blastocyst and will have many cells, usually more than 100. The best blastocyst is then transferred into the uterus on the fifth day following the egg collection. Extended culture gives us a greater chance of selecting higher quality embryos, which in turn leads to a higher rate of implantation. Furthermore, blastocyst transfer on day five mimics more closely the timing at which an embryo would reach the uterus in natural conception.

The risks of blastocyst culture include:

- 1) No embryos developing into a blastocyst resulting in no embryo transfer. Blastocyst culture is therefore only suitable for patients who have one-two good quality embryos depending on the number of eggs fertilised.
- 2) Increased risk of monozygotic (identical) twins following extended culture
- 3) Unknown long term risks of extended culture of embryos *in vitro*.

How are my embryos put back?

Two, three or five days after the egg collection you will have one or two of the best embryos transferred into the uterus through the cervix. You will need to have a full bladder at the time of the transfer. This is a painless procedure and does not require any anaesthetic. You will be required to remain horizontal for a short time after the embryo transfer and can then return home.

To support the womb lining to encourage implantation you will be asked to use progesterone pessaries vaginally twice a day starting the morning after egg collection. Additional Progesterone support may be advised.

Leicester Fertility Centre is unable to guarantee that your treatment will be carried out by a specific doctor. Please let us know if you would not like to proceed with treatment unless a specific doctor is available.

What happens with the other embryos?

We have the facility for embryo freezing and this will be offered to you to store suitable 'spare' good quality embryos for your own future use.

The use of eggs, sperm or embryos for training

At the end of your treatment cycle there may be unused sperm, unfertilised eggs and embryos that are unsuitable for freezing.

On your HFEA WT & MT consent forms you have the option to allow eggs/ sperm/ embryos to be used for training purposes prior to their discard. You can either tick 'no' in which case the eggs/ sperm/ embryos that were not used in your treatment will be discarded or you can tick 'yes'. If you are being treated with your partner then you both must agree on what is to happen to your embryos.

If you tick 'yes' for training then nothing will be done until the end of your treatment cycle. You can withdraw your consent at any time prior to their use in training. There is no financial benefit from consenting for your eggs/ sperm/ embryos for training. Selecting either 'yes' or 'no' for the use of your sperm/ eggs/ embryos for training will not impact on the care you receive.

Your consent forms will be checked prior to treatment and your wishes will be logged on the laboratory paperwork. If, at the end of your treatment cycle, the eggs/ sperm/ embryos are to be used for training purposes then two members of the embryology team will recheck the HFEA WT and MT consent forms to confirm that valid consent is in place.

Any eggs/ sperm/ embryos to be used in training will be transferred to a new container and kept in a separate incubator space to any eggs/ sperm/ embryos in use. A log is kept of all eggs/ sperm/ embryos used

for training, including which staff member has used them and for what technique. The eggs/ sperm/ embryos could be used for the purpose of training staff in embryo biopsy, embryo storage or other embryological techniques as per the HFE Act 2008 (for example moving embryos or eggs from one dish to another or egg injections). We would not attempt to create any embryos when training with eggs and sperm. The gametes would also not be used to 'test' or 'validate' equipment as per the HFE Act 2008. Patients using donor sperm and/or donor eggs may / may not be able to donate their embryos for training depending on what the donor has consented to. If you wish to find out if your donor has consented to training, please speak to a member of the clinical team. As not all eggs/ sperm/ embryos available from patients who consented to training are required by staff, it is not guaranteed that samples will always be used in training. If you would like to know, after your treatment cycle is complete, you can ask if your samples were used and for what technique.

Once the training has been completed the eggs/ sperm/ embryos would be discarded and not used for any other purpose. By allowing your eggs/ sperm/ embryos to be used for training you are helping the embryologists and patients of tomorrow and we thank you for your help.

When can I do a pregnancy test?

You will be given a date to carry out a urine pregnancy test at home and to contact the unit with the result.

1. If your test is positive you will need to collect further medication and have a blood test the following week.
2. If negative but your period has not started, a blood test will be organised that day to confirm the urine result.
3. If negative but your period has started, a follow-up appointment will be arranged.

What risks are involved?

The egg collection involves sedation anaesthesia and therefore it is important that you tell us about any other medical conditions that you have or medication that you may be taking.

Anaesthetic side effects include postoperative nausea and vomiting (usually last for 1-2 hours and can be controlled with medications), postoperative shivering, chest infection (very rare with sedation anaesthesia), awareness (becoming conscious during some part of operation; the majority of patients who are aware do not feel any pain, but may have memories of events in the operating theatre), allergic reaction to anaesthetic, very rarely anaphylaxis (risk is 1 in 10,000), risk of death or brain damage during anaesthesia (in general the risk is 1 in 100,000 but should be even rarer in sedation for minor procedures)

There is a very small risk of pelvic infection after the egg collection. Symptoms include fever, moderate to severe lower abdominal pain or malodorous vaginal discharge (rare).

Vaginal bleeding/Vaginal laceration requiring stitches (very rare)

Injury to bowel, bladder, pelvic blood vessel or nerve (very rare)

When ICSI is carried out there is a risk of damage to the eggs (approximately 5-10%) due to the injection procedure. Damaged eggs cannot be used for treatment. Very rarely, some eggs or embryos could be lost by accident due to human error.

Cancelled cycles due to poor or excessive response to the drugs
Failure of eggs to fertilise (IVF or ICSI) which would result in the cancellation of your cycle

Failure of embryos to cleave (divide) which would result in the cancellation of your cycle

Failure to transfer embryo via the cervical route

Ectopic Pregnancy

Multiple pregnancy - the risk of multiple pregnancy (mainly twins) after transferring two embryos is 20-30%. The risk of monozygotic (identical) twins after IVF is 1.5%. Monozygotic twins occur even after transfer of a single embryo. Multiple pregnancies carry more risks to the mother and baby. See leaflet about multiple pregnancy for more information.

Common side effects of medication

Suprecur: Tiredness, headache, hot flushes, irritability and injection site irritation – redness, swelling, bruising or pain.

Gonadotrophins: Headache, tiredness, nausea, vomiting, diarrhoea, abdominal discomfort, bloating and injection site irritation – redness, bruising, swelling or pain

Multiple pregnancy. OHSS – see section below

Hcg Trigger (Ovitrelle) – Headaches, tiredness, Breast pain, Diarrhoea, local skin reactions at the injection site, abdominal discomfort, bloating, nausea and vomiting.

Multiple pregnancy. OHSS – see section below

Doxycycline: (an antibiotic to be taken for 5 days after egg collection to help prevent any infection developing)

May cause nausea, vomiting, diarrhoea, oesophageal irritation and photosensitivity.

Progesterone: Drowsiness, Abdominal discomfort and or distention, constipation, breast pain, hot flushes.

Please read the information leaflets provided with your medication and if you have any concerns please discuss with the nurses

Ovarian hyperstimulation syndrome (OHSS):

OHSS occurs when there are too many follicles produced in the ovary. In severe cases, which are fortunately rare, fluid can collect in the abdomen and chest causing discomfort and difficulty in breathing. This may lead to a greater tendency for the blood to clot causing thrombosis.

How do I know if I'm developing OHSS?

The following are the symptoms that you may develop as a result of OHSS:

- **Mild OHSS** – mild abdominal swelling or bloating, abdominal discomfort and nausea. You will be advised to drink plenty of oral fluids at home and report to us if you have other symptoms or if your symptoms get worse.
- **Moderate OHSS** – symptoms of mild OHSS but the swelling and bloating is worse because fluid is building up in the abdomen. There is abdominal pain and vomiting
- **Severe OHSS** – symptoms of moderate OHSS plus extreme thirst and dehydration because so much fluid is building up in the abdomen, passing very small amounts of urine which is very dark in colour (concentrated), difficulty breathing because of build-up of fluid in the chest and a red, hot, swollen and tender leg due to a clot in the leg or lungs (thrombosis).

If you develop any of these symptoms then you should contact the Fertility Specialist Nurses on 0116 258 5922. If outside clinic hours please use the emergency mobile number on the answer phone

What will happen then?

ACU staff will arrange for you to be reviewed by the nursing and medical staff in the ACU during working hours or at the Gynaecology Assessment Unit (GAU) at the LRI out of hours. Sometimes it is necessary to recommend admission to hospital to closely monitor and observe you. It may be necessary to give you blood-thinning injections to prevent clotting and transfusion of intravenous fluids to encourage the kidneys to produce urine in normal amounts. Rarely, if there is a large fluid collection in the tummy and/or chest that has to be drawn off to improve comfort.

If admission is recommended, you really must be admitted. Since IVF commenced in the UK there have been a few UK deaths related to OHSS.

Can anything be done to stop me developing OHSS?

At the time of the final scan (before the hCG injection) we will have made a fairly accurate estimate of the number of eggs that are likely to be collected on the day of retrieval. You will be told if we think you are at increased risk of developing OHSS. Rarely, we may decide to cancel your egg collection if we think that the risk of developing severe OHSS is very high. In this case we will ask you to stop your gonadotrophin injections and continue with the Suprecur for 2 weeks.

Occasionally, when a high number of eggs is expected along with very high level of your hormone we may decide to do egg retrieval with no embryo transfer. This will be based on your symptoms and clinical judgment. IVF will be carried out in the embryology laboratory and all suitable embryos will be stored by freezing for your future use in subsequent months. You may be placed on a medication which reduces the risk of OHSS called Cabergoline given for eight days from the day of hCG injection.

Sometimes, although your hormone levels are high and we anticipate a high number of eggs, we may still be able to continue with egg collection and embryo transfer, and may prescribe Cabergoline (as mentioned above). We will give the prescription from the hospital and the medication needs to be collected from the hospital pharmacy. There are no major side effects of this medication.

What are treatment 'add ons'?

Add ons are optional extras that may be offered on top of your normal fertility treatment. They are emerging techniques that may have shown some promising results in initial studies but haven't necessarily been proven to improve fertility outcomes; such as pregnancy or birth rates.

Our clinic does not charge for the add ons embryo glue & time lapse monitoring. The cost is included with our treatment packages as standard. To make it easier to identify which add ons have evidence supporting their effectiveness and safety and which have very little evidence, or should be considered experimental, the HFEA have created a three colour traffic light rating system, consisting of the following colours:

- **GREEN:** an add-on which has more than one high quality randomised control trial (RCT) which shows that the procedure is effective at improving the chances of having a baby for most fertility patients.
- **AMBER:** an add-on where there is conflicting evidence from RCTs to show that an add-on is effective at improving the chances of having a baby for most fertility patients. This means that the evidence is not conclusive and further research is required,
- **RED:** an add-on where there is no evidence from RCTs to show that it is effective at improving the chances of having a baby for most fertility patients.

More information about add ons and what the most up to date traffic light rating is for each individual add on can be found at the HFEA website: <https://www.hfea.gov.uk/treatments/treatment-add-ons/>

Embryo glue

Embryo glue contains a natural substance called hyaluronan, which may improve the chance of the embryo implanting in the womb. It is added to the solution in the dish in which the embryos are kept before being transferred to the woman.

Are there any risks?

There are no known risks from using embryo glue.

What's the evidence for embryo glue?

Research from Cochrane reviews shows that embryo glue containing hyaluronan increases pregnancy and live birth rates by around 10%. There is one high quality study in this review which shows that the use

of embryo glue improves pregnancy and live birth rates. Other studies in the review were of moderate quality. Further high quality studies are needed before doctors can be confident of the benefits of embryo glue.

Endometrial scratching

In order to have a successful pregnancy, an embryo needs to 'implant' in the womb; if it doesn't, the woman will need to start her cycle again. Most embryos don't implant because they've been unable to develop fully to the implantation stage or because of a developmental mismatch between the stage of the embryo and the lining of the womb.

However, in a small number of cases an embryo won't implant because the lining of the womb isn't providing them with the right environment. Endometrial scratching is carried out before IVF and is intended to correct problems with the womb lining. During the procedure the lining of the womb (the endometrium) is 'scratched' using a small sterile plastic tube.

The theory is that this procedure triggers the body to repair the site of the scratch, releasing chemicals and hormones that make the womb lining more receptive to an embryo implanting.

Some research suggests the treatment may activate genes that make the womb lining more receptive to an embryo implanting.

Are there any risks?

There is a small risk that if you have an infection within your cervix before 'scratching', this may cause the infection to spread up into the uterus. Your clinic can treat this if necessary.

What's the evidence for endometrial scratching?

Early results suggest that endometrial scratching could increase pregnancy rates, although stronger evidence is needed to prove this.

Time-lapse imaging

In IVF, time-lapse imaging is used to help select the embryos most likely to successfully develop into a baby.

In conventional IVF, the embryologist will check the developing embryos each day under a microscope, which involves removing them from the incubator for a brief period.

Time-lapse imaging allows the embryologist to take thousands of images of the embryos as they grow without disturbing them. Not only does this mean the embryos do not have to be removed from the incubator, it also allows the embryologist to get a continuous view of each embryo as it develops, rather than just viewing them once a day. The embryologist can then choose a specific embryo for implantation based on criteria such as rate of development and the number and appearance of cells. Indeed, being undisturbed while they grow may improve the quality of the embryos.

Are there any risks?

No, there are no known risks to the woman or her embryos from time-lapse imaging.

What's the evidence for time-lapse imaging?

There have been various studies to try and see if time-lapse imaging can improve birth rates. Initial research has shown some promise, but it's still very early days.

There's certainly not enough evidence to show that time-lapse imaging improves birth rates, which is something you may want to consider if it's being offered to you at an extra cost.

Pre-implantation genetic testing for aneuploidy (PGT-A)

PGT-A involves checking embryos for abnormalities in the number of chromosomes. Embryos with an abnormal number of chromosomes (known as aneuploid embryos) have less chance of developing into a baby or, less commonly, may result in a baby being born with a genetic condition. PGT-A identifies aneuploid embryos that are unsuitable for fertility treatment.

For more information relating to the risks and the evidence for PGT-A, please refer to our Pre-implantation genetic testing for aneuploidy (PGT-A) patient booklet.

What follow up care is available after our IVF or ICSI cycle?

We would normally offer you and your partner a follow-up telecom appointment if your treatment has not been successful. We understand that this is a very difficult time for you both emotionally. Should you wish to access any supportive counselling during your fertility treatment you may wish to contact the Leicester Fertility Centre to arrange an appointment with the unit's counsellor.

Our commitment to patients

We are constantly striving to improve our services to patients and we will welcome your comments or suggestions for improvement.

Leicester Fertility Centre Contact Details

Tel: 0116 2585922
E-mail: LFCinfo@uhl-tr.nhs.uk
Website: www.leicesterfertilitycentre.org.uk

Useful addresses

Human Fertilisation and Embryology Authority: www.hfea.gov.uk
NICE guidelines: www.nice.org.uk
NHS - Response line: 111.nhs.uk / 111
NHS - Smoking helpline: 0300 123 1044
Fertility Network UK: www.fertilitynetworkuk.org / 0121 323 5025
SEED (Sperm, Egg & Embryo Donation) Trust: www.seedtrust.org.uk

Do you feel that you are at risk of verbal or physical abuse? If so, you may find the following numbers useful:

Domestic Violence Helpline:

United against violence & abuse (UAVA)

Helpline: 0808 802 0028

Email: info@uava.org.uk

Text support: 07715 994 962



This information was correct at the time of printing. While the Trust makes every reasonable effort to keep its information leaflets up to date, very recent changes may not be reflected in the guidance and you should discuss this with the clinical staff at the time of your appointment.



Today's research is tomorrow's care

We all benefit from research. Leicester's Hospitals is a research active Trust so you may find that research is happening when you visit the hospital or your clinic.

If you are interested in finding out how you can become involved in a clinical trial or to find out more about taking part in research, please speak to your clinician or GP.

If you would like this information in another language or format, please contact the service equality manager on 0116 250 2959

إذا كنت ترغب في الحصول على هذه المعلومات في شكل أو لغة أخرى ، يرجى الاتصال مع مدير الخدمة للمساواة في 0116 250 2959.

আপনি যদি এই লিফলেটের অনুবাদ - লিখিত বা অডিও টেপ'এ চান, তাহলে অনুগ্রহ করে সার্ভিস ইকুয়ালিটি ম্যানেজার ডেভ বেকার'এর সাথে 0116 250 2959 নাম্বারে যোগাযোগ করুন।

如果您想用另一种语言或格式来显示本资讯，请致电 0116 250 2959 联系“服务平等化经理” (Service Equality Manager)。

જો તમને આ પત્રકમાં જુદાં ભાષામાં અથવા ટેપ પર ભાષાંતર જોઈતું હોય તો મહેરબાની કરી સર્વિસ ઈકુવાલિટી મેનેજરનો 0116 250 2959 ઉપર સંપર્ક કરો.

यदि आप को इस लीफलेट का लिखती या टेप पर अनुवाद चाहिए तो कृपया डेव बेकर, सर्विस इक्वालिटी मैनेजर से 0116 250 2959 पर सम्पर्क कीजिए।

Jeżeli chcieliby Państwo otrzymać niniejsze informacje w tłumaczeniu na inny język lub w innym formacie, prosimy skontaktować się z Menedżerem ds. równości w dostępie do usług (Service Equality Manager) pod numerem telefonu 0116 250 2959.

ਜੇਕਰ ਤੁਹਾਨੂੰ ਇਸ ਲੀਫਲੈਟ ਦਾ ਲਿਖਤੀ ਜਾਂ ਟੇਪ ਕੀਤਾ ਅਨੁਵਾਦ ਚਾਹੀਦਾ ਹੋਵੇ ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਡੇਵ ਬੇਕਰ, ਸਰਵਿਸ ਇਕੁਆਲਿਟੀ ਮੈਨੇਜਰ ਨਾਲ 0116 250 2959 'ਤੇ ਸੰਪਰਕ ਕਰੋ।

Ak by ste chceli dostať túto informáciu v inom jazyku, alebo formáte, kontaktujte prosím manažéra rovnosti služieb na tel. číslo 0116 250 2959.

Haddaad rabto warqadan oo turjuman oo ku duuban cajalad ama qoraal ah fadlan la xiriiir, Maamulaha Adeegga Sinaanta 0116 250 2959.