



## In-vitro fertilisation (IVF)

### What is In-vitro fertilisation (IVF)?

IVF is a process by which eggs are fertilised by sperm outside of the womb (in-vitro). The embryo (fertilised egg) is then transferred into the womb to achieve pregnancy or is cryopreserved (frozen) for future use.

### What does this involve?

Prior to IVF, you and your husband would need to undergo screening for infectious diseases. You would also undergo an ultrasound assessment of the pelvic organs, assessment of the cavity of the womb, trial cannulation (insertion of a catheter into the vagina and cervix to find the path into the womb) if necessary, and a mapping of your hormonal profile to assess your ovarian reserve to have a gauge of how well you might respond to hormonal medication. Hormones and other medications may then be administered to increase the number of eggs available for harvesting by stimulating the development of multiple follicles (which contain the eggs) in the ovaries. This process may take 2 to 3 weeks, and regular transvaginal ultrasound scans are performed to assess response to this treatment. On rare occasions where the ovary is deemed unlikely to respond to this, the eggs are harvested based on your natural cycle instead. We refer to this as natural cycle IVF.

The eggs are retrieved using an ultrasound-guided needle, either transvaginal or transabdominal, from follicles in the ovaries. This is an outpatient procedure, where a sedative and painkiller are usually given to make you relax and go into a light sleep. This will last for about half an hour to an hour. Usually, the husband will have to submit a fresh semen sample in person, unless there are stored frozen sperm. The eggs are then incubated with the sperm in a dish in the laboratory to allow natural fertilisation in conventional IVF. Alternatively, Intra-Cytoplasmic Sperm Injection (ICSI) can be performed where a single sperm is injected into the egg to assist in fertilisation. The resulting embryo(s) is incubated in the laboratory where the embryologists will select the most suitable embryo(s) for transfer.

The embryos may be transferred between Day 2 to blastocyst stage of embryo development depending on the medical team's decision, e.g., by considering the quality and number of embryos available. As the embryos develop from Day 2 to blastocysts, the number of embryos will be reduced. The purpose of culturing the

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embryos to blastocysts stage is to allow selection of better embryos and may result in the reduction of the number of embryos available. To transfer the embryo to your uterus, the embryo is placed in a catheter which goes through the vagina and the cervix. The process takes about half an hour.

The Singapore Ministry of Health permits a maximum of 2 embryos to be transferred at any one time. Rarely, under special circumstances, 3 embryos may be transferred (e.g., in women at least 37 years of age and has undergone one or more stimulated cycles in which no eggs were collected or from which no egg collected developed into a blastocyst). Embryos that implant successfully will result in a pregnancy. If there are any good quality embryo(s) remaining, the patient can choose to have them frozen for future use, donated, or disposed. The completion of an IVF cycle varies generally from 4 to 7 weeks. Eggs that are not fertilised and embryos that are not transferred or cryopreserved due to abnormality or poor quality will be disposed.

### **What precautions must I take for the procedure?**

Please inform your doctor if you have any medical illnesses. Before the procedure, please inform your doctor if any of the following are applicable:

1. You have a history of allergy or reaction to any medications, drugs, or food.
2. You have a history of bleeding or clotting disorders.
3. You are taking drugs (e.g., Aspirin, Clopidogrel, Warfarin, and Rivaroxaban) or supplements (e.g., Cordyceps, Ginkgo Biloba, and Lingzhi), that thin your blood, as these substances may affect blood clotting and increase the risk of bleeding. If you are taking any of these, your doctor will advise you accordingly.
4. Ensure that your medical condition(s), if any, is/are under control.

### **What are the risks and complications of the procedure?**

#### **A. The IVF cycle may need to be abandoned due to the following reasons:**

##### **1. Too many follicles developing**

There is an approximate 3 – 8% risk that too many follicles may develop. The cycle may need to be abandoned because of risk of developing Ovarian Hyperstimulation Syndrome [OHSS (refer to below)]



## **2. Insufficient follicular development or no oocyte retrieved**

Follicular development is unpredictable. The risk of none or insufficient follicular development is around 2%. In such an event, the treatment cycle may have to be abandoned before the eggs can be retrieved. The risk that no eggs are recovered at the point of egg retrieval is about 1%.

## **3. Poor or no fertilisation or poor embryo development**

This occurs rarely. If this occurs, the cycle may be abandoned. In some patients, we would offer an ICSI (intracytoplasmic sperm injection) in a subsequent cycle.

## **4. Failure or difficulty in transferring embryos**

Embryo transfer could sometimes be difficult or unsuccessful due to anatomical variations. This may require the patient to wait for a fuller bladder, or the doctor to use a stiffer catheter and/or require the doctor to use a tenaculum (instrument to hold the cervix). Sometimes, you may require sedation. Failure to transfer the embryos is extremely rare.

## **B. Unavailability of sperm on the day of oocyte retrieval**

1. In the rare event that sperm is not available (due to poor survival of frozen sperm or husband being unable to produce semen sample), retrieved oocytes may be frozen for use in future cycles (a separate consent form will be signed if that occurs).

## **C. Risks and complications associated with hormone stimulation**

### **1. Ovarian Hyperstimulation Syndrome (OHSS)**

There is approximately a 1% risk of the patient suffering Ovarian Hyperstimulation Syndrome (OHSS), which may result in kidney failure, deep vein thrombosis (formation of blood clots in the leg veins) and pulmonary embolism (dislodgement of blood clots in the lungs). Pulmonary embolism is potentially life threatening. To minimize the risk of deep vein thrombosis and pulmonary embolism, blood thinning medication may be given if OHSS develops. Sometimes, to avoid the possibility of OHSS, the embryos are frozen and transferred at a later time when the risk of OHSS has resolved.

2. **Multiple gestational pregnancy** (12 –18% based on number of embryo transferred)

All the embryos transferred may result in successful implantation and hence, multiple gestational pregnancy may occur (pregnancy with twins or more). It is also possible for an embryo to split into two and result in



identical twins. This may pose certain risks to the fetus(es) and mother, such as the following:

- Risks to the fetus(es) include increased risk of miscarriage, preterm labour and prematurity as well as attendant complications which require care in the intensive care unit (ICU) such as respiratory distress, brain damage, including loss of life.
- Risks to the mother include higher risks of morning sickness (nausea and vomiting), miscarriage, caesarean section, preterm delivery, hypertension, anaemia, and diabetes. The mother will also be at greater risk of social, psychological, and financial stress during and after delivery. You are advised to see the Medical Social Worker and/or Psychiatrist if necessary.

### 3. Adverse drug reaction

Some patients may experience unwanted, uncomfortable, and sometimes dangerous effects from the medications used (adverse drug reaction). Although uncommon, this may necessitate admission to the hospital for further observation or treatment.

## D. Risks and complications associated with Oocyte Retrieval and Embryo Transfer

### 1. Bleeding

Due to the nature of the procedure, bleeding could occur. Although uncommon, this may require blood transfusion, hospitalisation for further observation and/or treatment.

### 2. Infection

Infections following egg retrieval are not common. Severe infection may require hospitalisation for intravenous antibiotics or surgical treatment. This may complicate your reproductive treatment and lower the chances of successful conception.

### 3. Perforation of the uterine wall

This could occur during the introduction of the catheter when transferring the embryo(s). This may be treated conservatively and/or with an antibiotic course, and hardly ever require surgery.

### 4. Injury to nearby organs

In the process of egg retrieval from the ovary, the needle may injure nearby organs. This rare complication may require hospitalisation for intravenous antibiotics or surgical treatment.

### 5. Failure of embryo implantation

Even after the embryo(s) has been transferred, it may fail to implant into the uterus, and hence pregnancy may not occur.

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## E. Risks and complications inherent in any pregnancy

### 1. Risks associated with older patients

Pregnancy rate is lower for women above 40 years old and there is a higher risk of developing complications, such as hypertension, diabetes, or delivery requiring caesarean section. For women above 35 years old at the estimated date of delivery, there is also an increased risk of genetic anomalies in the fetus, e.g., having a baby with Down's Syndrome.

### 2. Risks of ectopic pregnancy, miscarriage, and fetal abnormality

There is also a risk of ectopic pregnancy, i.e., pregnancy occurring outside the normal cavity of the uterus (2 – 11%). Compared to natural pregnancies, there is also a higher rate of miscarriage (12 – 30%) and a higher risk of fetal abnormality (5.5%). This is thought to be due to the underlying problems in a subfertile couple rather than the IVF procedure itself.

## What can I expect after the procedure?

Usually, medical leave is prescribed for approximately two weeks from the date of embryo transfer until the blood pregnancy test is taken. During this time, it is advisable to avoid intercourse or vigorous exercise. However, complete bed rest is discouraged. Hormonal medication will be prescribed to support the pregnancy. You may experience spotting vaginally before the blood pregnancy test is done. This may be due to the embryo(s) implanting in the womb or impending menses.

## Psychosocial Support

Fertility treatment may have an impact on your emotional and mental well-being. During treatment, you may experience a range of emotions and may find difficulty managing them. Do inform your healthcare professional if you would like to speak to a counsellor at any time before or during the treatment process.

## What are my other options?

1. The option of no treatment.
2. Surgery in endometriosis (the tissue growth beyond or outside the uterus resembling the inner lining of the uterus). Endometriosis is known to cause subfertility and surgery will be to remove cysts in the ovaries or affected tissue.

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However, endometriosis can recur, and repeated removal of cysts may reduce remaining ovarian tissue and ovarian reserve.

3. Laparoscopic ovarian drilling, injection to stimulate ovulation, or lifestyle changes to achieve weight loss in some cases of Polycystic Ovarian disease. Polycystic Ovarian disease is a common cause of anovulation (i.e., difficulty with egg release) and usually fertility drugs would have been used as the first line of treatment.

4. Use of donor semen in men who have no, or extremely low sperm count in ejaculation or after failed surgical retrieval.

5. Use of donor egg in women who have poor ovarian reserve or response to IVF stimulation.

6. Intrauterine insemination in mild male factor infertility where fallopian tubes are patent.

7. Child adoption when it is deemed the chances of success of IVF are very poor or not acceptable.

8. You can discuss the options in more detail with your doctor.