



S A M A A

FERTILIZATION CENTER

A guide to In Vitro Fertilization (IVF) and Intra Cytoplasmic Sperm Injection (ICSI)


مركز سماء للأخصاب
Samaa Fertilization Center

IVF & ICSI Treatment Stages

IVF/ICSI treatment is divided into the following:

- Investigation and assessment
- Ovarian stimulation
- Egg collection
- Fertilization
- 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 prepared. 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 desensitized (suppression) and stimulation of the ovaries commence.

Fertility drugs

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

1. **Gonadotropins (FSH/LH)**: these are known as stimulation injections as they stimulate the ovary and encourage the antral follicles to start growing. There are different preparations called *Gonal F* and *Fostimon*, all of which contain the same primary drug called follicle stimulating hormone (FSH).

2. **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.

3. **Trigger injections: (*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.

Ovarian Stimulation

Once your treatment plan has been confirmed 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 taken for between 10-14 days. The injections are administered just under the skin, usually in the abdominal area (around the belly button). The response to the FSH injection is monitored through regular scans and blood tests. During ovarian stimulation *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 estrogen (E2) blood test may also be performed. Depending on the progress of the follicles, the dose of the medication may be adjusted.

Important to note

During ovarian stimulation many follicles may grow though some may not produce an egg. Neither the scan nor the estrogen blood test can give an indication if there are eggs inside the follicles. This can be confirmed only at the time of egg collection once the contents of follicular fluid have been examined by an embryologist.

How do the follicles grow?

The response of the follicles in the ovary differs from patient to patient. 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 are decided following a review of the results of all the pre-treatment tests in addition to any previous IVF cycles undertaken by the patient. 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 trigger injection is usually given 36 hours before the egg collection, therefore always administered in the evening by the patient. The trigger must be taken at a specific time as timing is crucial from this point onwards.

Points to be noted during ovarian stimulation

- The hormones must be injected daily around the same time. This may continue from approximately 10 to 14 days.
- 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

A semen sample which is used to fertilize the egg is usually collected on the same day. We will ask the husband to abstain from ejaculation for at least three days and not have a long period of abstinence (over 7 days). 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 specified room at the Samaa Fertilization Center. In certain cases,

a sperm sample can be produced at home with prior consent and arrangement.

Egg Collection

During the egg collection follicular fluid-filled sacs in the ovary are aspirated and the eggs are isolated in the embryology lab. It is a day case procedure performed at the Samaa Fertilization Center in the morning. You arrive at the Samaa Fertilization Center at between 7.30-8am where you will be seen by the nurses followed by your consultant. The anesthetist will reassess you, checking your name and date of birth along with the embryologist. A small cannula will be placed on your hand and sedation is given through your vein. This is not a general anesthetic hence the recovery is much faster, 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. 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:

- You will be required to fast (nothing by mouth) from the midnight before your schedule egg collection.
- You may take a shower in the morning.
- Avoid wearing any make-up, nail varnish or jewelry.
- 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 nausea. 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.

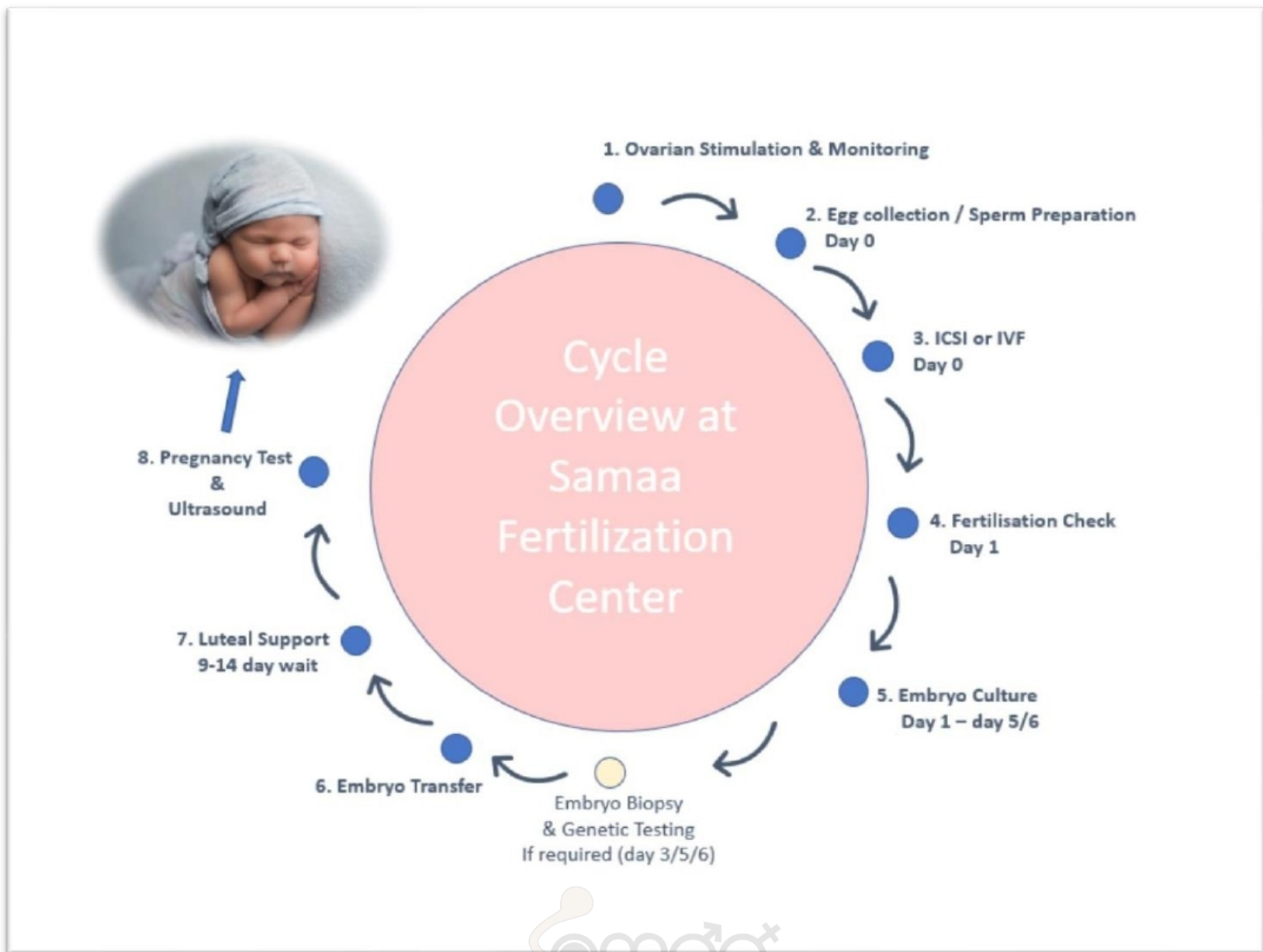
Fertilization

The eggs are fertilized by either IVF or ICSI. A sperm sample must be prepared prior to any of these procedures and will normally indicate which procedure we will be following.

With IVF, the sperm is washed and mixed with the eggs in a dish and incubated overnight. ICSI involves selecting a single sperm and injecting into the egg under a high-powered microscope.

Retrieved eggs will either be mature (MII) or immature (MI & germinal vesicle – GV). Mature eggs have completed the segregation process where certain chromosomes are discarded, thus making them ready for fertilization. Immature eggs have not had the segregation of chromosomes and have double the number of chromosomes and hence cannot be fertilized. Germinal vesicles have not yet gone through the process of egg formation and are discarded. The proportion of mature and immature egg varies from patient to patient; older women and those with polycystic ovaries tend to have a higher number of immature eggs.

If ICSI treatment is planned, the cells around the eggs are removed to check for maturity. Immature eggs cannot be injected with sperm. The next morning a fertilization check takes place, during which an embryologist looks at all the eggs that have been inseminated to see if normal



fertilization has occurred. Fertilized eggs are called embryos, and these embryos should start to divide in the days following fertilization. This division is morphologically assessed by an embryologist.

Normal embryo development:

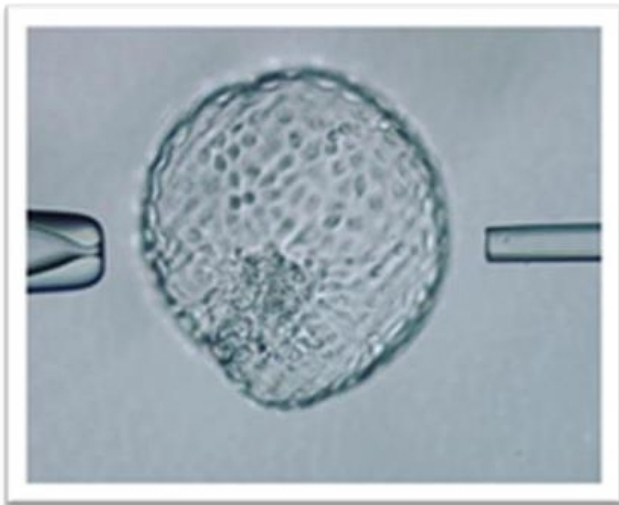
Day 1: a single cell with two pro-nuclei (PNs)

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: the blastocyst stage, an embryo containing 100 to 150 cells with a fluid filled cavity. The blastocyst is made up of two types of cells – the external cells called trophoblast which will ultimately form the placenta and other pregnancy support structures and the inner cell mass (ICM) which will form the fetus.



It is important to note that not all embryos become blastocysts. Approximately 20-30% of all fertilized eggs may become a blastocyst but this may vary with age (increasing age yields less blastocysts), egg reserve as well as sperm quality. A blastocyst culture is planned if there are more than 3 good quality embryos on day 3 (i.e. 8 cells and above). Sometimes blastocyst culture may not be advised, and embryos may need to be frozen or transferred at an earlier stage.

Assessment of embryos is based only on morphology (how they look). Good quality does not confirm genetic normality and 40% (<30 years) to 80% (>40 years). In order to confirm a normal genetic constitution preimplantation



genetic testing would have to be carried out (this must be pre-arranged).

IVF Complications

IVF has been carried out for 40 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 is the most common risk of IVF. Multiple pregnancies could lead to complications during gestation (increased risk of miscarriage) and are at risk of pre-term labor.

With IVF there is also a higher chance of having an ectopic pregnancy

Ovarian hyperstimulation syndrome (OHSS)

This is one of the most serious complications and it increases when more than 10 to 15 follicles are growing with high estrogen levels. Patients with polycystic ovaries are at a higher risk of developing OHSS. In rare cases, where the response is extremely high, the cycle may need to be cancelled to prevent OHSS and protect the

patient. OHSS symptoms include severe abdominal pain, swelling, nausea, vomiting and shortness of breath. If you experience any of these symptoms, please contact the emergency number provided. Some patients with OHSS 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.

Injury to bowel, bladder and bleeding

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

Embryo Transfer

Embryo transfer is performed 3 or 5 days after the egg collection and depending on the progress the embryos are making. Frozen embryo transfer may also be offered in cases where there are available frozen – thawed embryos from a previous cycle. In a fresh cycle we assess the embryos depending on the number of cells and the grading. One or two of the best embryos are chosen, and they are transferred with the help of a very small catheter, using a technique very 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.
- ✓ 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 the blastocyst (day 5 or 6) stage can be frozen following MoH approval.

How long can embryos be frozen?

Embryos can be frozen up to 5 years and in special circumstances this time period can be extended further. The laboratory charges a yearly fee for storage which is paid directly to the Samaa Fertilization Center. Should you decide you no longer require your embryos to be kept in storage a signed consent form by both the husband and wife will be required in order to discard the embryos.

Pregnancy test

If a test is positive, we ask you to continue all the medications and arrange a scan with your fertility specialist. 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.



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