

Intra Cytoplasmic Sperm Injection (ICSI)



**AUSTRALIAN
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ICSI is a procedure whereby a single sperm is artificially inserted directly into an egg instead of penetrating the egg in the normal way. If the egg fertilizes, the resulting embryo is then placed into the woman's uterus.

Who considers ICSI?

ICSI may be used in the following circumstances:

- Male factor infertility
- The avoidance of transmission of infectious diseases e.g. HIV
- For cases where fertilization was not successful using IVF
- In cases where only one or two eggs are available for fertilization
- Men with a blockage
- Men who have had a vasectomy.
- Gender selection (Family Balancing)

Approximately one man in 25 has sperm qualities which make it impossible for him to father children normally.

About 13% of these men have untreatable infertility many having no sperm at all. Some do produce sperm which are either not motile (do not swim) or do not have the normal shape and structures which are required for normal penetration of eggs. These men, plus a further 10% who have either very low sperm counts, very low percentage of motile sperm or a very large percentage of their sperm being abnormally shaped, and those men whose sperm do not adequately

fertilize eggs in normal IVF would be likely to benefit from ICSI.

Where couples who have tried IVF and no fertilization (or only occasional fertilization) was achieved and where the cause of this reduced fertilization rates can be attributed solely to the poor fertilizing ability of the sperm, then couples will be offered ICSI.

Couples, where the male's sperm count is extremely low may be advised by their gynecologist to attend a Genetic Counselling session before commencing treatment.

The basic stages involved in the ICSI procedure are similar to IVF and are detailed below;

- Suppression of the natural cycle
- Growth and maturation of several eggs
- Monitoring egg development
- Trigger injection
- Collection of the eggs
- Injection of each of the eggs with one sperm
- Transfer of the embryo into the uterus
- Progesterone treatment and pregnancy test
- Further treatment cycles

Suppression of the natural cycle

Medications used to suppress the cycle can either be started one week before the period is due (long down regulation cycle), the day after onset of the period (Flare Cycle) or when serial ultrasound indicates appropriate timing for

commencement (Antagonist Cycle). These medications are Lucrin and Synarel, which belong to a group known as Gonadotrophin Agonists, or Orgalutran and Cetrotide, which belong to a group known as Gonadotrophin Antagonists. Use of these medications allows control of the cycle and accurate timing of oocyte collection which dramatically improves the success of oocyte collection.

At present it is not known whether ART procedures such as ICSI or IVF increase the risk of a child being born with a congenital abnormality. Many research studies have examined this issue but conflicting results have been presented. In a study of nearly 6000 children born after IVF or ICSI, researchers in Belgium did not observe any increased risk of major malformations or neonatal complications. In a smaller study from Western Australia the researchers reported an observed increase in abnormalities in children born after ICSI and IVF.

Whether the observed increase in this study is due to the treatment procedures or parental fertility related issues is not known, although recent reports suggest that parental factors might be involved.

For men whose infertility is caused by a condition known as "Y chromosome micro deletion" there is an increased risk that this condition will be inherited by their sons after ICSI.

Stages involved in an ICSI cycle

Stimulation of the ovaries

In this stage medication is taken to help the ovary to develop a number of eggs.

Collection and insemination of the eggs

This procedure is usually done under light anaesthetic. The eggs and fluid are gently removed from the surrounding follicles and the eggs are then injected with washed and treated sperm from the male partner.

Embryo development

The fertilized eggs are placed into embryo culture dishes and then into specially designed embryo incubators. The embryo development is checked daily until the time of the embryo transfer.

Embryo transfer

This is a minor procedure lasting about fifteen minutes. Embryos can be transferred to the uterus 2, 3, or 5 days after fertilization.

Embryo storage

Embryos that are not transferred can be cryopreserved and stored for use in subsequent frozen embryo transfer cycles.

Growth and maturation of eggs

In the IVF/ICSI cycle medication, given by injection, is used to stimulate the ovaries to develop a number of eggs compared with a natural cycle where usually only one egg is produced.

The drugs used to stimulate egg production may be Puregon or Gonal F. Sometimes other medications are also added for example Clomiphene Citrate (Clomid) or Pregnyl.

Multiple factors impact upon the exact prescription that will be administered to an individual. Your specific treatment plan will be decided between you and your gynecologist.

Monitoring egg development

The eggs (oocytes) develop in follicles, which are small fluid filled cysts or sacks growing in the surface layer of the ovary. As the eggs mature the follicles increase in size and produce increasing amounts of estradiol (an estrogen hormone). By monitoring estradiol levels with serial blood tests (usually starting day 8 of the cycle) and follicle size and number by ultrasound, the maturity of the developing eggs can be tracked. Once the eggs are considered mature the HCG trigger injection (see below) will be arranged.

Blood tests

Blood tests have to be done between 7.30am and 9.00am so that the results are available the same day. This can be done at the main Concept Fertility Centre.

Ultrasound examination

These scans are done at Concept Fertility Centre between 0800am and 0830am. Ultrasounds are usually performed vaginally and no full bladder is needed. It is important to note that the number of eggs collected may differ from the number of follicles seen on ultrasound.

Trigger injection

HCG (human chorionic gonadotrophin) is a hormone which

performs the function of the naturally occurring LH (Luteinizing Hormone) surge, triggering the final maturation of the eggs and ovulation. This is referred to as the trigger injection. This is given by subcutaneous injection 34- 36 hours before the egg collection is planned.

It is extremely important that this injection is given at the exact time planned as failure to do so will result in no eggs being collected.

If you make a mistake with the timing of your trigger injection it is important to inform the coordinator doctor. A trigger injection is always required in IVF/ICSI cycles.

There is no "correct" estradiol level to reach before trigger injection as there is enormous variation between patients. The pattern of blood and ultrasound results interpreted together determine whether the response to treatment is good. In general, however, it is important that the estradiol level rises steadily until the eggs are collected. It is very important to realize that a wide range of individual treatments are used in the program. Please do not be alarmed if your treatment is different from someone else's. The aim is to design the best individual protocol for you.

Collection of eggs (Ovum Pick-up)

This is most commonly done using a vaginal ultrasound probe under a light anesthetic, although intravenous sedation can be used as an alternative, depending on the patient's preference. In certain circumstances the collection may be done laparoscopically, in which case a general anesthetic is used. The follicles are visualized by ultrasound, and the fluid inside them is sucked through a needle and tubing into a test tube. The tube is passed immediately to the embryologist who looks for the egg under the microscope. The eggs are then put into the incubator. You can be discharged 2-4 hours after the

Operation. When possible, your own gynecologist will perform the egg collection, but because of other commitments this is not always Possible.

Sperm collection

We will inform you of the approximate sperm collection time once the ovum pick-up time has been arranged. It will be around the time of the operation. Two to three days abstinence from intercourse prior to egg collection is advised to obtain an optimal sample.

It can be very difficult for some men to produce a sperm sample on request under these conditions. If you are worried about this aspect of the program, please discuss it with us at or before the start of the treatment cycle, so that arrangements can be made to freeze some semen if necessary - semen freezing must be done at least a week before egg collection.

Sexual activity may be continued as usual until two to three days before the time of the egg collection. Abstaining from then on is important to allow the sperm to reach optimum quality.

For men who have had a vasectomy or have a blockage sperm can be retrieved directly from the epididymis or the testis. This is done under anesthetic just prior to the egg collection procedure.

Events in the laboratory

The sperm sample is washed and then injected into the eggs, 4 hours after egg collection. The eggs are kept in culture dishes in an incubator until next inspected 16-18 hours later. At this time they are checked under the microscope to determine whether fertilisation has occurred.

Embryo Transfer

You will need to contact the Coordinator daily so we can inform you of the progress of your Embryos. Transfer of the embryo into the uterus will be between Day 2 after fertilization up until Day 5 at which stage the embryo is called a Blastocyst. No more than 1 or 2 embryos will be transferred because of the risk of multiple pregnancies.

This is a minor procedure, usually requiring no anesthetic, which will be undertaken by your gynecologist unless they are committed elsewhere. It is a little like having a pap smear performed, a speculum is passed into the vagina, the cervix is washed with fluid that is non-toxic to embryos and then an outer catheter is placed into the cervical canal. Once your doctor is happy with the positioning, the embryologist will bring through your embryo loaded in a second catheter. This catheter is then passed through the outer catheter. Once the doctor is happy with the positioning of this catheter, the embryo is expelled into the uterus. The procedure takes approximately 15 minutes. After transfer you will be asked to rest for 1/2 hour.

Progesterone and pregnancy blood test

The hormone progesterone is needed to help the embryo attach to the wall of the uterus and development of the placenta. During an IVF/ICSI cycle progesterone is administered via progesterone pessaries, Crinone Gel or less often by Pregnyl injections. This will be started on the day of egg collection.

You will be given instructions after your embryo transfer regarding your blood test(s) and medications. Other blood tests, specific to your cycle which are ordered by your doctor will also be on your post-operative instruction sheet. Menstruation does not necessarily mean that a pregnancy is not developing.

Intracytoplasmic Sperm Injection (ICSI)

One sperm is injected directly into the egg.

You must continue blood tests until a final outcome is known.

The blood test taken approximately two weeks after your egg collection will detect whether the pregnancy hormone (HCG) is present and check your blood progesterone level. If the pregnancy hormone is detected it is too early to know whether there is a healthy continuing pregnancy. Further blood tests and an ultrasound examination are needed.

Unfortunately ICSI, like natural conception, can lead to a chemical pregnancy (transient rise in pregnancy hormone followed by a late period), miscarriage or ectopic

(tubal) pregnancy, as well as the happier outcomes: so a positive blood test is not the end of the waiting.

Multiple pregnancy (twins or triplets) are more common with ICSI than with natural conception if 2 embryos are replaced. A single pregnancy is safest for both the mother and the baby. The number of embryos to be replaced should be discussed at each treatment with your doctor.

Repeat ICSI attempts

If pregnancy is not achieved then a repeat attempt can be made after a full menstrual cycle has elapsed. This break is important to ensure a good response and reduce the risk of side effects in future treatment cycles.

The next treatment cycle may involve blood test hormone tracking for frozen embryo transfer or a further ICSI cycle depending on individual situations.

Please make review appointments with your gynecologist well in advance to avoid delays in progression of your treatment.

For more information on what to expect in a treatment cycle please see the patient information sheet entitled "Risks And Side Effects of ART medication and procedures".

Birth outcomes following ICSI

ART procedures such as ICSI or IVF increase the risk of a child being born with a congenital abnormality. Many research studies have examined this issue but conflicting results have been presented. In a

study of nearly 6000 children born after IVF or ICSI, researchers in Belgium did not observe any increased risk of major malformations or neonatal complications. In a smaller study from Western Australia the researchers reported an observed increase in abnormalities in children born after ICSI and IVF.

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Benefits of ICSI

ICSI has been shown to achieve fertilisation rates of about 70%, similar to that of IVF.

ICSI has resulted in pregnancy rates which are similar to IVF Success rates.

These rates depend to a large extent on:

- Age of the woman
- The woman infertility status and cause
- Number of embryos replaced

Disadvantages of ICSI

A small number of eggs might be damaged during the ICSI procedure. Should this happen these will not continue to fertilise or develop into embryos.

Whilst there is evidence from a study in Brussels that the incidence of abnormalities in children resulting from ICSI procedures is no greater than in the normal population, there may indeed be an increased risk of abnormalities using ICSI. We cannot say categorically that these risks will be at the same rate as in the "normal" population. Please refer to the patient information sheet titled "Risks & Side Effects associated with ART Technologies 12.1.10".

There is an additional fee for ICSI.

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