

Sims Fertility Clinic		Form No.	PT-INFO-017
Revision No.	01	Effective Date	07/07/2009

ICSI Information

ICSI

What is it and are there risks?



sims IVF

For the past several decades, the number of people seeking medical advice for fertility related issues has been increasing. Throughout the world, over 300,000 children have now been conceived using IVF techniques. The first pregnancies from intracytoplasmic sperm injection (ICSI) were reported in 1992 in the medical journal the Lancet. Since then tens of thousands of children have been born as a result of this procedure.

What is ICSI?

ICSI is similar to conventional IVF in that gametes (eggs and sperm) are collected from each partner. The difference between the two procedures is the method of fertilisation. With conventional IVF, the sperm and eggs are mixed together in a dish and the sperm fertilise the eggs “naturally”. With ICSI a single sperm is picked up using a fine glass needle and is injected directly into an egg (See Figure 1). In both IVF and ICSI, the eggs are incubated overnight and examined for fertilisation the next morning. Fertilised eggs (zygotes) are cultured in the lab for 2 to 6 days at which time the resulting embryos can be transferred back into the uterus of the woman. It is important to note that some of the eggs collected may not fertilise. This can be due to several factors, the eggs may not be mature enough, they might not be of high enough quality and with ICSI, they may not survive the injection process. Live birth rates for ICSI and conventional IVF are similar.

When is ICSI used?

ICSI bypasses the natural processes involved in a sperm penetrating an egg and is therefore used when there are problems that make it difficult to achieve fertilisation naturally or with conventional IVF. Circumstances in which ICSI may be appropriate include:

- When sperm count is very low.
- When the sperm cannot move properly or are in other ways abnormal.
- When sperm has been retrieved surgically from the epididymis (PESA), or the testicles (TESA/TESE), from urine or by electro-ejaculation.
- When there are high levels of antibodies in the semen.
- When there has been a previous fertilisation failure using conventional IVF.

Men who fall into the above categories where there are very few sperm in their semen (oligozoospermia), have sperm that do not move correctly (asthenozoospermia), have high numbers of abnormal sperm that are unable to naturally fertilise an egg (teratozoospermia) or even a combination of problems would previously have had little chance of fathering their own genetic offspring. ICSI offers these men and their partners the real chance of having a genetically related child.

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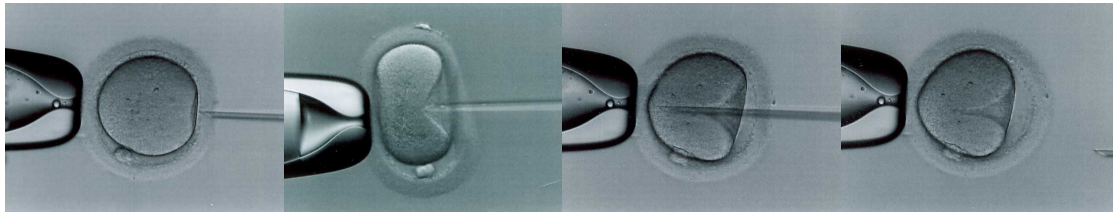


Figure 1. Illustration of the ICSI procedure.

The egg is held in position with suction from the holding pipette (on the left). The injection needle holding the sperm is then introduced and the sperm injected.

What are the risks of ICSI?

An ICSI treatment cycle like an IVF treatment cycle is an invasive procedure and as such carries the risks associated with any invasive medical procedure. However, unlike IVF, ICSI involves injecting a sperm directly into an egg, therefore allowing the use of sperm that may not have otherwise been able to participate in fertilisation. For these reasons, concerns about the potential risks to children born as a result of ICSI have been raised, and a range of follow-up studies published. ICSI is still a relatively new technique and all of the children conceived using ICSI are still very young. Consequently, these studies cannot include effects that may only be seen in adulthood or even in the subsequent generation. There are however some risks that must be considered:

Possible inheritance of genetic and chromosomal abnormalities.

Chromosomal defects and the inheritance of subfertility.

Abnormal numbers or structures of chromosomes, particularly the sex chromosomes (X and Y), may be associated with infertility in both men and women. As it is impossible to tell if a sperm or egg is chromosomally abnormal by physical observation babies born via ICSI may have a slight increased risk of inheriting these abnormalities. It has been shown that up to 6.1% of fathers and 4.8% of mothers enrolled in an ICSI program have some form of chromosomal abnormality compared to 3.0% in fertile controls.

A small portion of subfertile men have parts of the Y chromosome missing (microdeletions). Certain genes on the Y chromosome have been shown to be involved in the production of sperm (spermatogenesis), and deletion of these genes may be the reason these men have few or even no sperm in their semen. Consequently, using sperm with such microdeletions to create an embryo may result in the same type of subfertility being passed from father to son (only males carry the Y chromosome).

The complexity of egg and sperm production means that even if an individual possesses a normal number of chromosomes, their gametes may not. It is impossible to detect which eggs or sperm have these abnormalities and gametes that may not have fertilised naturally may be used for ICSI.

Overall, it does seem that the offspring resulting from ICSI do indeed have an increased risk of chromosomal abnormalities. In the majority of cases, these abnormalities stem from the underlying risks of inheritance from the parents and are generally minor.

Inheritance of cystic fibrosis gene mutations.

Some men who have no sperm in their semen are found to have congenital bilateral absence of the vas deferens (CBAVD). In this condition, the tubes that carry the sperm from the testes to the penis are missing. Two thirds of men with CBAVD are also carriers of certain cystic fibrosis mutations. **Men with CBAVD and their partners are therefore advised to consider genetic testing and counselling before proceeding with ICSI.**

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Possible birth and developmental defects.

Birth defects.

Determining whether or not ICSI causes higher numbers of congenital defects at birth as compared to conventional IVF or natural conception has proved somewhat contradictory over the past 10 years. Some studies have shown increases in defects whilst others have not. The problems have stemmed from the many confounding factors present in such studies. For example maternal age (patients receiving fertility treatment tend to be older than those conceiving naturally and abnormalities increase with age), multiple births (there are a higher number of multiple births following IVF and ICSI with malformations more likely in a multiple birth), the classification of major and minor defects (various birth registers class certain birth defects major when other registers would class them as minor) and the probability that those children being followed up after ICSI are actually examined more thoroughly therefore, picking up defects that would be routinely missed during normal post-natal checks, have all been shown to influence the result of studies. However, when the confounding factors are taken into account and adjusted for, the current consensus within the scientific community is that **there appears to be no increased risk of congenital abnormalities following ICSI.**

Developmental Defects

As with birth defects, reports on developmental defects have been contradictory with many confounding factors. Again however, the current general consensus is that when all other factors are taken into consideration there appears to be no difference in development between children conceived via ICSI, IVF or naturally.

Possible risks during pregnancy.

Miscarriage

There does appear to be a slightly higher risk of miscarriage with both ICSI and IVF pregnancies as compared to natural conceptions. This again may be due to abnormal gametes being used that would not normally create an embryo. However most abnormal embryos would not implant into the womb, but some might, therefore leading to this slightly higher miscarriage rate.

Conclusions.

Intracytoplasmic sperm injection appears to be a safe alternative for couples who would otherwise be unable to achieve a pregnancy. There does not seem to be any inherent risks with the physical procedure itself. However, ICSI could allow abnormal gametes to be used thereby passing on genetic or chromosomal abnormalities from parents to child.

Further Reading.

Matthew G et.al. Is intracytoplasmic sperm injection safe? Fertil Steril 2003; 80: 851-59