

THE HULL IVF UNIT



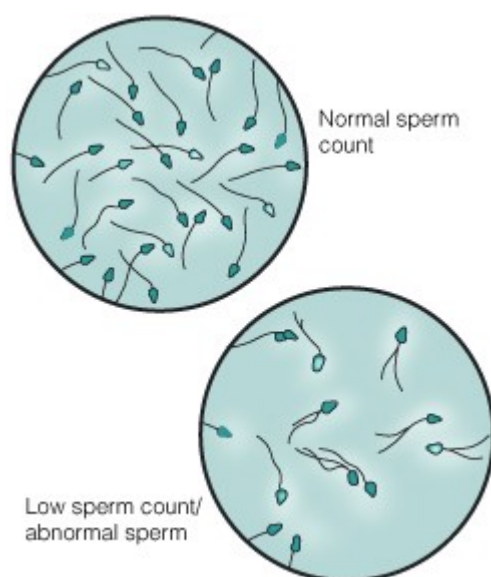
Patient information on Intracytoplasmic Sperm Injection

Introduction

In-vitro fertilisation (IVF) is widely used in the treatment of couples with male infertility problems. Even IVF may fail in certain couples where the male-factor infertility is severe. Many couples are unable to conceive because of a sperm problem – insufficient numbers of sperm which may have an abnormal appearance, and are unable to move or function properly. In these cases, although the woman is producing good eggs, fertilisation may not occur. Thus, certain couples cannot be accepted for standard IVF treatments.

Who is ICSI suitable for?

In couples with an apparent sperm disorder the recommendation to perform ICSI is decided upon in advance of commencing treatment, following detailed discussion between the couple and the medical/scientific staff. The most common reason for performing ICSI is due to a reduced sperm count.



The count may be reduced if:

- Production in the testis is impaired
- There is an obstructive problem which cannot be overcome, in which case the sperm can be aspirated from the epididymis or the testis itself.
- A freeze/thaw sample results in much diminished numbers.
- There is a reduced availability of sperm due to other reasons such as retrograde ejaculation of sperm into the bladder.

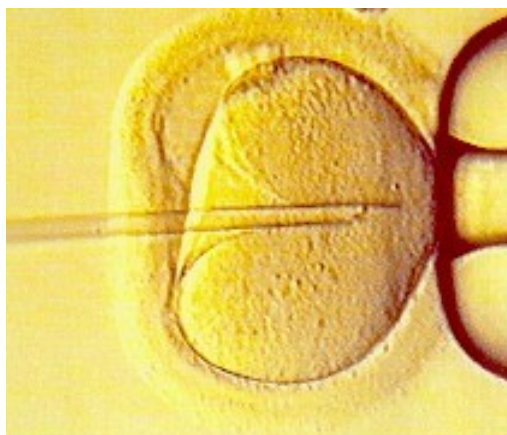
Occasionally the semen sample may be of borderline normal/abnormal quality and a split IVF/ICSI treatment cycle may be recommended. Once the eggs have been divided into two groups i.e. eggs to be submitted to standard sperm exposure in standard IVF, or to ICSI, the eggs can not be moved to the other group. This is to prevent the risk of genetic material from more than one sperm entering the same egg – this might not initially be obvious if eggs submitted to standard IVF and had apparently failed to fertilise were then submitted to ICSI. Oocytes (eggs) 24 hours old or more, will not be used for treatment using ICSI because the oocyte chromosomes will become more centrally located after 24 hours and thus, with ICSI, there is an increased risk of dispersal of the chromosomes.

In couples who have experienced unexpected failed fertilisation with standard IVF, all eggs in subsequent cycles are subjected to ICSI. Fertilisation rates of about 75% can be expected with standard IVF but of course there is much variation between individuals. Occasionally there is unexpected complete failure of fertilisation, but this can occur as a chance event. If sperm function is known to be defective, the proportion of eggs fertilised (called the fertilisation rate) will be relatively low on average. There will be complete failure more often than usual, but some will do unexpectedly well. However, the embryos that are produced have a relatively low chance of successfully implanting. This finding appears to be due to adverse (toxic) effects of abnormal non-fertilising sperm around the egg. In these cases, ICSI achieves not only a much better chance of fertilisation, but also of successful implantation. It would therefore be preferable to choose ICSI in the first place, rather than standard IVF, if there is doubt about sperm dysfunction. In borderline cases it would be reasonable to try standard IVF first and change to ICSI in a fresh cycle only if there was failure or only a low fertilisation rate.

How does ICSI work?

Failure of fertilisation using standard IVF is usually due to the sperm being unable to penetrate the outer membrane (zone pellucida) and the inner membrane (vitelline membrane) of the egg. Among the micromanipulation techniques tried to provide an answer to this problem, Intracytoplasmic Sperm Injection (ICSI) has proved the best. ICSI involves taking a single sperm and injecting it directly into the woman's egg, through both the surrounding membranes.

The eggs are obtained using the same drug stimulation and recovery techniques used in IVF. Instead of each egg cell being exposed to approximately 100,000 sperm cells in a plastic dish, in ICSI only one sperm is injected into each egg cell. Thus ICSI can be performed with only very few sperm, and many less sperm than would be required for standard IVF.



A sperm is aspirated into a fine glass 'needle' which is several times finer than a human hair. Using micromanipulation equipment the needle is passed through the outer layer of the egg (the zone pellucida) then the egg cell membrane, so that the sperm can be placed in the cytoplasm of the egg cell.

Only one sperm must be injected to avoid introducing an abnormal amount of genetic material into the cell. (In a natural cycle, although hundreds of sperm try to penetrate the egg, a normal egg cell will only allow one sperm to enter). All the other natural steps in the fertilisation process now have to occur. This can fail, but on average about 75% of the eggs treated by ICSI can be expected to fertilise. A maximum of 2 of the resulting embryos can be transferred back into the uterus, as in an IVF cycle.

Risks involved with ICSI

It is very important to remember that, while ICSI has been available since 1992, it is still considered a fairly new form of treatment and there are many follow up studies of the resulting babies being carried out.

The following are specific areas of concern:

Cystic Fibrosis

In males with congenital bilateral absence of the vas deferens, ICSI is likely to result in an increased incidence of cystic fibrosis in the offspring. Men who have congenital absence of the vas deferens will be screened for the genes responsible for cystic fibrosis; their female partners will also be screened.

Specialist genetic counselling will be offered when an abnormality of chromosomes is found. Pre-natal diagnosis should be considered by the couple if pathology is found.

The options and risks of fetal loss following pre-natal diagnosis can be discussed with the Unit's medical staff and also the specialist genetic counselling staff. (Only a limited number of centres, and Hull is not one, offer pre-implantation diagnosis).

Y Chromosome Deletions

One explanation for abnormalities in sperm function is that there are small pieces of genetic material missing from the male Y chromosome. It is currently not known whether or not this problem will be transmitted to any male off-spring.

Sex Chromosome Anomalies

In males with sperm problems there is an increased risk of a sex chromosome disorder in their children. These chromosome abnormalities are relatively frequent in the whole population (1:700) and are usually undetected. Affected male off-spring may have similar fertility problems to their fathers. If an abnormal chromosome complement is found in a male partner, genetic counselling will be offered prior to treatment.

Birth Defects

Embryos resulting from ICSI treatment appear to have normal development potential in culture and pregnancies after ICSI have no less chance of proceeding than for conventional IVF. So far, there is no clear evidence that ICSI results in higher rates of major birth defects. Careful genetic analysis of pregnancies and follow up studies after delivery are continuing.

Studies suggest that minor abnormalities occur in up to 20% of ICSI babies, compared up to 15% of the population.

The number of babies reported to have a major congenital defect is between 1% and 5% following both natural conception and ICSI.

Inherent defects in male chromosomes, especially the sex chromosomes, may be more likely to be passed on to male offspring with the use of ICSI, when compared to natural conception and standard IVF, because of by-passing the natural selection process by the two egg cell membranes.

Developmental Delays

Initially it was thought that there may be evidence for developmental delays in children born as a result of ICSI treatment. This concern has not been borne out by bigger, longer term studies which have recently been published.

These concerns about ICSI will be discussed with you prior to treatment. As new information is becoming available all the time, we will be glad to update you at the time of your treatment.

ICSI Success Rates

The national success rates for IVF and ICSI are comparable, both in terms of embryo development, embryo quality and pregnancy outcome, and the data from the Hull IVF Unit supports this. In 2007, 48% of all IVF treatment was represented by ICSI cycles.

Hull IVF Unit: IVF/ICSI Statistics

Hull IVF Unit clinic data is displayed below:

Treatment cycles started	Live birth rates for all ages 2009	Clinical pregnancy rates for year 2010
IVF only (per embryo transfer)	29.0% (61/210)	35.4% (68/192)
ICSI only (per embryo transfer)	27.8% (35/126)	43.5% (50/115)

We, at the Hull IVF Unit, consider that ICSI should be an option available to couples where this form of assisted conception may be appropriate. ICSI permits fertilisation for couples who would be unable to generate embryos without this additional intervention step to aid the process. The resulting fertilisation rates are comparable to those quoted for patients having conventional IVF treatment.

Choosing ICSI as an Option

If ICSI is considered an option for a couple, the couple will have a discussion about this with the medical/embryology staff.

This will involve:

- An explanation of the technique involved
- Chances of success
- Risks involved
- Costs (is it more time consuming and costlier than IVF).