Intracytoplasmic sperm injection (ICSI)

Before ICSI became a routine treatment in the mid-1990s, men with sperm problems had very little chance of fathering their own children. This is because poor quality sperm is likely to achieve very low fertilisation rates when standard IVF is used, even if egg quality is high. However, where IVF requires many millions of sperm cells for in vitro fertilisation, ICSI requires just one, injected by a skilled embryologist.

Today, improved investigation and diagnostic procedures, including tests to assess the genetic integrity of sperm cells, provide much more reliable indications of sperm quality and a better basis for determining the appropriate treatment strategy. In addition, surgical sperm retrieval techniques mean that men with no sperm cells in the ejaculate (azoospermia) can still be suitable for ICSI provided that a small number of viable cells can be retrieved from the testis and surrounding tubes.

Once injected, the eggs are incubated overnight as in conventional IVF, after which time the embryologist checks for evidence of fertilisation.

Success rates
We have been performing ICSI for many years, with many thousands of procedures completed and thousands of healthy babies born. The average normal fertilisation rate is currently around 70% after ICSI. While ICSI does not absolutely guarantee fertilisation, the rate of complete failed fertilisation is very low and is most common in cases with limited egg supply. Live birth rates after ICSI are comparable with those of conventional IVF and are largely dependent upon the age of the female partner and the cause of infertility.

When is ICSI appropriate?
- When patients have too few sperm for conventional IVF
- When there is very low sperm movement (motility)
- When there are high levels of abnormal sperm present

Is ICSI safe?
There have been many scientific studies investigating the possibility that birth defects are increased with the use of IVF in general, and ICSI specifically. There is general agreement that further research is necessary before any firm conclusions can be reached, and these studies continue to be done. What is established for certain is that the possibility of birth defects is low in all cases and that the risks are not great. You should, however, be aware of the concerns.

Damage to eggs
ICSI is an invasive technique and eggs may occasionally be damaged during the procedure. This happens in less than 5% of injected eggs and damaged eggs are never used in treatment.

Of equal or even greater concern are the risks associated with poor sperm quality which are summarised below.

Genetic problems
A small number of men with very low sperm counts have pieces of genetic material missing from their Y chromosome. These men risk passing on this defect to male children, who would also have fertility problems later in life.
life. However, there are no reports that other aspects of health are affected. Men considering ICSI will be offered a specific genetic analysis, if appropriate, prior to ICSI.

**Cystic fibrosis**
It appears that 5 – 10% of men with no sperm in their ejaculate have congenital absence of the vas deferens (the tubes through which sperm travel to form an ejaculate). Up to 70% of men with this condition are also carriers of the cystic fibrosis gene mutations. Couples considering ICSI will therefore be offered screening for cystic fibrosis.

**Birth defects and developmental delay**
While it is still too early to be absolutely sure that the ICSI procedure itself does not cause problems for babies and children, the results of early studies are very encouraging. Several large studies have shown that ICSI babies and children are no worse off than those conceived following natural conception. Follow-up studies are ongoing and will study older children and, ultimately, the next generation after ICSI. Results from one big study indicate that children born after ICSI and natural conception show comparable cognitive and physical development at the age of 10 – a conclusion which mirrors the same positive findings at ages 5 and 8.

**Surgical sperm retrieval**
An uncommon type of infertility (affecting 1 – 2% of the male population) occurs where the male partner has no sperm in the semen (azoospermia).

In around half these cases sperm production by the testes is normal but there is a blockage which prevents sperm entering the semen (obstructive azoospermia). This may be because of:

- Failure of the sperm passages to develop (congenital absence of the vas deferens)
- A blockage of the sperm transport tubules (epididymis or vas deferens)
- A previous vasectomy operation (male sterilisation)

Although many vasectomies and sperm blockages can be corrected, the surgery is unsuccessful in a significant proportion of patients. At present there is no certain method of reconstructive surgery to offer men with congenital absence of the vas deferens.

In the other 50% of cases there is inadequate sperm production by the testes – either a congenital problem or the result of injury, previous disease (such as mumps) or x-ray treatment. In these patients sampling (biopsy) of the tissue of the testis reveals that many men (about 30 – 40%) have areas where there are normal sperm which do not pass into the semen, even though there is no blockage.

The minimally invasive techniques of PESA or TESE, usually performed under local anaesthetic combined with a sedative, are used in these cases.

**PESA (percutaneous epididymal sperm aspiration)**
A fine needle is inserted into the epididymis at the upper area of the testis and sperm cells are obtained by gentle suction.

**TESE (testicular sperm extraction)**
A fine needle is inserted into the testis and samples of tissue are obtained by gentle suction to retrieve enough sperm. If too few sperm are obtained, a biopsy (tissue sample) is taken through a small incision and two or three stitches are placed in the skin. These self-dissolve in about ten days.

PESA and TESE provide an opportunity of fatherhood to some sterile men who would otherwise remain childless. The chance of successful pregnancy and delivery of a baby is similar to that of conventional ICSI.

**After sperm retrieval**
Patients are generally informed on the same day whether sperm has been found or not. However, in the most difficult cases a two to three day period of tissue incubation is necessary before sperm can be recovered. Recovered sperm with normal motility and morphology will be frozen for later use. There are generally enough sperm to perform several ICSI cycles.

The chance of recovering sperm by PESA or TESE is almost 90% if there is a simple blockage. With abnormalities of the testes the average recovery rate is around 50 – 60%.
After the procedure there will be a little bruising and tenderness of the scrotum for a day or two. Any stitches will self-dissolve in 10 – 14 days and healing may be aided by taking twice-daily five-minute baths with small amounts of added salt or disinfectant.

All surgical procedures carry a small risk of bleeding, pain, bruising and wound infection but in practice most patients are back to full activity within two or three days. Taking regular painkillers such as paracetamol or ibuprofen as prescribed by the surgeon will help with any discomfort.

**Sperm preparation and ICSI**

Following the procedure the sperm is prepared for ICSI. However, because azoospermia is associated with some inherited abnormalities, some additional testing is usually necessary.

**Genetic abnormalities?**

Genetic defects on the Y (male) chromosome present a particular problem as they will inevitably be transmitted to sons. Recently, certain genes necessary for the development of sperm have been isolated (known as DAZ genes) and it is now known that the absence of these genes can be anticipated in approximately 10% of men with severe sperm problems. Men with non-obstructive azoospermia having TESE will therefore be advised to have a test to check for gene deletions on the Y chromosome. The obvious risk for the male offspring is infertility or sterility, apparent only in adulthood.

**Cystic fibrosis testing**

Two in three men with cystic fibrosis (CF), a serious congenital illness leading to severe respiratory problems in infants, will have congenital absence of the vas deferens. In such cases we test both the male and female partner for CF gene mutations, which can be detected in blood or saliva. If the male is a carrier of the CF mutation but the female partner’s test is negative, the risk of their baby developing CF is 1 in 300 – whereas in the general population the risk is about 1 in 600. Specialist genetic counselling is recommended and this can be arranged by the clinic. However, if both partners are positive, preimplantation genetic diagnosis (PGD) would usually be recommended.