

## InfoSheet : INTRA-CYTOPLASMIC SPERM INJECTION (ICSI)

### INTRODUCTION

A variety of problems can occur during the many steps involved in the journey of a sperm from the male genital tract to fertilizing an egg in the woman's fallopian tube. Infertility is not a problem that affects only women, 40% of all infertile couples have male factors that contribute to the cause of their infertility. In the past, there was very limited treatment and success for those couples with significant male factor infertility.

In the early 1990s, a revolutionary technique known as intra-cytoplasmic sperm injection (ICSI) was first described and has been widely available in most IVF clinics since the mid 1990s. ICSI now allows couples with even severe male factor infertility to have genetically related offspring.

The couples who benefit from this technique are those with one or a combination of the following factors:

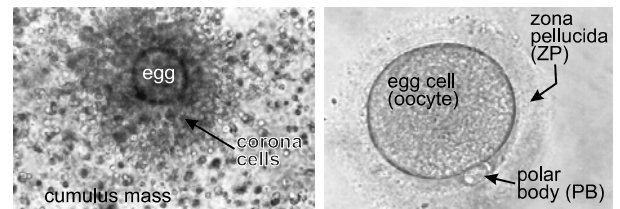
- low sperm count
- low sperm motility
- a low percentage of normal-shaped sperm (poor sperm morphology)
- poor or failed fertilization in a previous conventional IVF attempt (see VFC InfoSheet on "Fertilization Failure with IVF and ICSI")
- high incidence of polyspermic fertilization in a previous conventional IVF attempt (where more than one sperm entered many of the eggs)
- occasional rare combinations of other factors which may make ICSI more favourable

In normal fertilization and conventional IVF more than a single sperm is required for an egg to be fertilized (contrary to popular beliefs). In IVF, each egg is usually exposed to approximately 100,000 sperm to ensure normal fertilization. In ICSI, a single sperm is injected into the egg, and therefore, theoretically, only one viable sperm from a semen sample is required for each egg.

ICSI involves many steps similar to a couple going through a "traditional" IVF treatment cycle. Hormonal stimulation and egg retrieval are the same. Production of the semen sample and

subsequent processing ("washing") of the sperm are basically the same (except in those few cases where surgical sperm retrieval is required). After ICSI, culture and handling of the embryos is exactly the same, and the embryos are also transferred back to the woman in exactly the same manner as those generated through IVF. The embryos generated by ICSI look exactly like those obtained by IVF.

The differences between ICSI and IVF are the method of fertilization (the sperm injection procedure) and the preparation of the eggs for this injection. When the eggs are removed from the ovary they are surrounded by a "cloud" of cells, this complete structure is referred to as the oocyte-cumulus-corona



complex (OCCC).

OCCC Egg (enlarged, cells removed)

### HOW IS ICSI PERFORMED?

#### Preparing the eggs

In order to perform ICSI, the cells surrounding the egg must be removed. Removal of these "cumulus" and "corona" cells ("stripping") is essential so that every aspect of the injection procedure can be seen clearly. Stripping also prevents the accidental insertion of any parts of these cells or their DNA into the egg during the injection procedure. Stripping is achieved by exposing the eggs briefly to an enzyme called hyaluronidase. This enzyme is found normally in the heads of sperm cells and, in normal fertilization, allows the sperm to "digest" their way through the cloud of cells to the egg. While the egg is in the hyaluronidase a series of small glass needles are used to aspirate it up and down to help remove the cells.

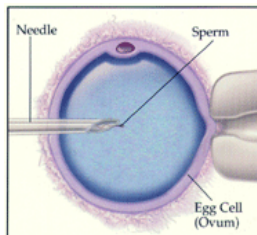
Most likely, all of the eggs obtained from an egg retrieval will not be of exactly the same quality. Occasionally one or more eggs may be unhealthy, immature or post-mature (these eggs in particular can be damaged during the stripping process). After stripping has been done the eggs are assessed for maturity. A mature egg, suitable for sperm injection, has a polar body present (see photograph, above). Eggs that are not mature will not be injected. Immature eggs do not have the correct number of chromosomes and the addition of a sperm will only result in an abnormal embryo that will not grow to form a fetus. After stripping and assessment of the eggs, the number of eggs suitable for ICSI is usually less than the number of egg masses (OCCCs) obtained at the egg retrieval.

### The injection procedure

Each mature egg is then injected with one sperm. The injection procedure is highly technical and requires very sophisticated and expensive equipment. ICSI also requires specially trained embryologists with years of experience being needed to perfect the technique. All this makes ICSI very expensive to provide, but also maximizes the results obtained.

The ICSI procedure is performed in the IVF laboratory, usually about 4 hours after the woman's egg retrieval procedure. A tiny glass needle called an "injection pipette" is used to isolate a single sperm from a small sample of prepared sperm. This sperm will be assessed for normal shape and motility (the quality and speed) or vitality (in the case of completely immotile sperm). The sperm is then immobilized by striking the tail quickly and carefully with the tip of the injection pipette. This breaks, but does not separate, the tail. The sperm must be immobilized so that it will not move once inside the egg because a swimming sperm will cause severe damage to the internal structure of the egg. The sperm is aspirated into the injection pipette tail first and the pipette is moved to the drop of medium containing the egg.

The egg is held in place and secured with another, larger, glass needle called a "holding pipette" (see



illustration, above). The injection pipette is then advanced to pierce the outer coating of the egg called the zona pellucida (see photographs,

above), and through into the middle of the egg. Suction is then applied through the injection pipette in order to break the very elastic membrane of the egg. Once the membrane has been broken, the sperm is gently deposited inside the egg cell and the injection pipette is removed. Remarkably, once the pipette has been removed, a normal healthy egg will resume its original shape in less than a minute.

Damage to eggs does occasionally occur during ICSI. The egg was not designed for, nor has evolved to be exposed to, this type of manipulation, and occasionally healthy looking eggs will be damaged by ICSI. Up to 15% of the eggs injected might suffer damage due to the technique itself (as reported worldwide). Depending upon the health and quality of the eggs, damage might or might not occur in any cycle with ICSI. The Victoria Fertility Centre accepts a damage rate of <5%, although very rarely a patient with poor quality eggs might see more damage.

Even though ICSI has revolutionized treatment for couples with male factor infertility, it will not guarantee a pregnancy. Every ICSI cycle, even for the same patient, can be different, with very different results. Even though the most up-to-date ICSI techniques are employed with the utmost care at all times, results do still vary and, due to the invasive nature of the technique and its potential for damage, success cannot be guaranteed.

### IS ICSI SAFE?

The oldest children born after the use of ICSI are not yet teenagers. Conflicting reports on abnormalities (or lack thereof) in IVF and ICSI children are constantly being published (see VFC InfoSheet on "Safety of IVF and ICSI"). This is because even though thousands of children have been born following ICSI, the numbers are still too small for final conclusions. So far the evidence suggests that the fetal abnormality rate is similar to that for the general population.

It is vital that couples understand the risks of ICSI and that the results concerning children born following ICSI are still inconclusive. Most of the abnormalities in ICSI children seem to come from cases with extremely low sperm quality, and some genetic abnormalities (including ones that cause male sterility) are transmitted via the sperm to the children. Also under current investigation in ICSI children, and IVF children in general, is the possibility of rare "imprinting" genetic disorders that cause developmental problems. If you have any questions on these issues, please ask your doctor.

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