



***In vitro* fertilization (IVF) & Intracytoplasmic Sperm Injection (ICSI) ©2005**

In vitro fertilization (IVF) is a procedure by which a woman's ovaries are stimulated with medication to produce multiple eggs at one time, so that the eggs can be collected by needle aspiration and fertilized in a laboratory. Embryos that appear to be developing normally can then be transferred back to the woman in hopes of achieving a pregnancy.

Intracytoplasmic sperm injection (ICSI) is a technique used during the IVF process to increase the success of the procedure. ICSI involves exposing all ripe eggs to an enzyme (hyaluronidase) to remove all nursing cells from around the egg. Then a single sperm is picked up in a fine, hollow needle and injected with a tiny amount of culture medium into the body of the egg (ooplasm). This technique increases the chance of successful fertilization.

There has been significant controversy with regard to what risks exist after a pregnancy is achieved through IVF and ICSI. A recent analysis of nineteen studies published since 1990 revealed that there is no difference in risk for major malformations when you compare IVF with ICSI to IVF with natural fertilization. When infants conceived through IVF and ICSI were compared to a control population of spontaneously conceived infants, there was a relative risk of 1.29 for major malformations in the IVF group. This means that there appears to be a slightly higher risk for major malformation in an IVF population, but more studies are needed to confirm and explain these risks.

With regard to chromosome abnormalities, the reported risks are 1.1-1.5% over the general population risk (0.5%) for spontaneous chromosome anomalies. The risk for chromosome abnormality has been reported to be associated with low sperm count, specifically concentrations less than 20×10^6 sp/ml, and decreased motility. The chromosome abnormalities observed however, may be benign and are therefore of no clinical significance. It is assumed that the above increased risks are due to the parental factors causing the infertility rather than the procedure itself, but this is yet to be confirmed.

Finally, assisted reproductive technologies (ART) have been associated with a reported increase in imprinting errors. Imprinting is the process by which a chromosomal segment receives a genetic "mark" according to the sex of the parent who contributed the segment. It is critical that embryos inherit information from both parents and that the cells are able to recognize the information through the imprinted "mark". If this process is disrupted, specific genetic disorders can result. One specific disorder, Beckwith-Wiedemann syndrome (BWS) has been observed in both animal and human studies. The cause for a higher rate of imprinting disorders is not clear, though recent articles have suggested an association with ovarian stimulation, type of culture media and length of culture time (specifically, to the blastocyst stage). There may be no difference in rates between IVF/ICSI and IVF with natural fertilization populations.

To address these risks, the authors of the above papers and many fertility centers advocate midtrimester prenatal ultrasound for the diagnosis of fetal malformations and recommend offering chorionic villus sampling (CVS) or amniocentesis for fetal karyotyping (looking at the baby's chromosomes). These recommendations are independent of any genetic testing done during the IVF process (preimplantation genetic diagnosis or PGD) due to the limited nature of this testing. CVS is associated with a 1% risk for pregnancy complications whereas amniocentesis is associated with a 1/300 (0.3%) risk for complications. Miscarriage occurs in approximately half of those cases with complications and clinic specific risks may vary. These tests assess for fetal chromosome abnormalities but do not allow for the diagnosis of all birth defects or genetic disorders.