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In vitro fertilization (IVF) & Birth Defect Risks

***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 injecting a single sperm 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. Several studies have suggested that there is no difference in risk for major malformations when IVF with ICSI is compared to IVF with natural fertilization. However, a systematic review of literature published on this subject until March 2003 inferred that infants conceived through **assisted reproductive technologies (ART)** had a higher incidence of birth defects as compared to a control population of spontaneously conceived infants. The risk for birth defects amongst the general population is 3-5%; the results of this systematic review estimates that the risk increases to 4-7% amongst infants conceived with ART. Ultimately, this means that there appears to be a slightly higher risk for birth defects amongst pregnancies achieved through ART, but more studies are needed to confirm and explain these risks.

With IVF, the reported risks for spontaneous chromosome abnormalities are increased (0.55% - 0.75%) over the general population risk (0.50%). This increased risk for chromosome abnormalities is assumed to be due to the parental factors causing the infertility rather than the IVF process itself, but this is yet to be confirmed.

Further, assisted reproductive technologies (ART) have been associated with a reported increase in imprinting errors. Imprinting is the process by which certain segments of genetic material are "marked" 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, the type of culture media used, and the length of culture time (specifically, to the blastocyst stage).

To address these risks, researchers, clinicians 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 less than 1% risk for pregnancy complications whereas amniocentesis is associated with a 1/1000 risk for complications. Miscarriage occurs in approximately half of those cases with complications (not all complications lead to miscarriage) 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. Specifically, imprinting errors would not be diagnosed. It is important to remember that not all birth defects are caused by chromosome abnormalities, and that not all birth defects are visible on ultrasound.

Health outcomes of children born via IVF and ICSI as they grow older are currently being investigated. Data available at this time imply that, while children conceived using ART may be at increased risk for health problems shortly after birth due to perinatal issues (prematurity, low birth weight, etc.), their health in general seems to be comparable to that of children conceived naturally throughout early childhood. More research is needed to confirm these findings and to investigate the health of these children throughout the lifespan.