CITY FERTILITY CENTRE
your partners in life

PRE-IMPLANTATION GENETIC DIAGNOSIS (PGD)

Pre-implantation Genetic Diagnosis (PGD), also known as Embryo Screening, is a state-of-the-art procedure used in conjunction with In Vitro Fertilisation (IVF). PGD is generally recommended to detect numerical or structural anomalies in the chromosomes of embryos. When embryos are affected by certain chromosomal conditions, these can prevent implantation to the uterine lining, lead to pregnancy loss, or result in the birth of a child with physical problems and/or mental disability.

PGD can help prevent adverse outcomes by identifying affected embryos as they are developing in the laboratory and before they are transferred to the womb during the IVF cycle.

PGD FOR ANEUPLOIDY

Normal human cells (i.e. embryonic cells) contain 46 chromosomes in 23 pairs. We receive 23 chromosomes from each parent. The first 22 pairs of chromosomes are the same for men and women. The 23rd pair determines our gender. A female has two "X" chromosomes, whereas a male has an "X" and a "Y". As such, the woman can only pass an X to her child in her egg. The man passes either the X or the Y in the sperm, therefore determining the sex of the child. If an error occurs, and the egg or sperm has an extra or missing chromosome, the embryo created by that egg or sperm will have an extra or a missing chromosome resulting in a condition called aneuploidy. Having an extra chromosome is known as trisomy (tri = three of a given chromosome) and having a chromosome missing is known as monosomy (mono = one of the chromosome). When aneuploidy involves the larger chromosomes, the embryo may not attach to the wall of the uterus or may stop developing soon after attaching and result in a miscarriage.

However, if the aneuploidy involves chromosomes such as the 13, 18, 21, X or Y, the pregnancy may still carry on until birth, even though the embryo has a chromosomal disorder. The most common of these is an extra number 21, known as Down Syndrome or trisomy 21 (three chromosome 21). Other common aneuploidies are Klinefelter Syndrome (XXY), trisomy 13, and trisomy 18. The features of the chromosome condition depend upon which chromosome is extra or missing, but can include physical differences and mental disability.

ANEUPLOIDY AND MATERNAL AGE:

As a woman advances in age, the chance of aneuploidy in her pregnancies increases because her eggs are also ageing. Females develop their total number of eggs while still in their mother's womb, and as a result, they are born with all the eggs they will have in their lifetime. In males, sperm is made every 65-75 days; therefore, the sperm is not as old as the man. Based on this, the theory regarding aneuploidy risk and advancing maternal age is that, over time, the chromosomes in the egg are less likely to divide properly, which results in the egg having an extra or missing chromosome. Therefore, the risk of aneuploidy increases with maternal age.

The purpose of PGD for aneuploidy is to select only chromosomally normal embryos for embryo transfer. The aim is to achieve pregnancies, fewer pregnancy losses and a reduced number of affected offspring.

HOW IS PGD PERFORMED ?

To test an embryo, one blastomere or embryonic cell is removed through a microscopic opening made in the outer protective membrane of the embryo. This takes place during the third day of development (5 to 8-cell stage). This is performed using microscopic pipettes and a laser by a highly trained scientist. The embryo is then kept in culture in an incubator while the cell's DNA is analysed.

THE PGD ANALYSIS

The biopsied cells are analysed using a technique called Fluorescence In-Situ Hybridisation or FISH. This technique uses probes, small pieces of DNA that are a match for specific chromosomes. Each probe is labelled with a different fluorescent dye. These fluorescent probes are applied to the biopsied cell and attach to the chromosomes. Under a fluorescent microscope, the number of chromosomes of each type (colour) can then be counted. The geneticist, therefore, can distinguish normal cells from cells with aneuploidy. The cell that is removed from the embryo for analysis is fixed to a glass slide and repeatedly heated and cooled in this process. As such, it cannot be used for another purpose or returned to the embryo. This analysis causes no extra inconvenience to the patient as it is accomplished in one to two days.

ADVANTAGES OF PGD

- **Reduction in the chance of having a child with Aneuploidy:** According to current figures, the chance of a woman delivering a baby with aneuploidy is on average 1% if she is 35-39 years of age and ~3.5% if she is 40-45 years of age. PGD does lower the chance of having an affected baby. However, the science does not yet allow us to test all of the chromosomes at present. We therefore

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and it is currently calculated at less than 1%. Other Assisted Reproduction procedures such as: Intracytoplasmic Sperm Injection (ICSI), Fragment Removal and Assisted Hatching are all performed by making microsurgical openings in the covering of the egg or embryo and none have been found to have other than mostly positive effects on implantation and viable pregnancy rates.

- **Removal of cells from the embryo:** No part of the future fetus will be affected because one or two cells are removed from an embryo approximately two days after fertilisation. At this developmental stage all cells in an embryo remain totipotent (until about the fourth day). These cells have not differentiated yet, meaning that each cell by itself could potentially grow into a whole and perfect fetus. The biopsy procedure merely delays continued cell division for a few hours, after which the embryo reaches the same number of cells as before and continues its normal development. It is possible that embryo biopsy may lower embryo implantation rates slightly, while selection of chromosomally normal embryos via PGD may increase them. Therefore, the balance between potential biopsy damage and beneficial effects of PGD seems to be positive.

- **Misdiagnosis:** The accuracy of PGD for aneuploidy is approximately 90%. This means that the error rate is 10%. Within this chance of misdiagnosis, there is a false negative rate, a false positive rate, the chance for no result and the chance for mosaicism. Mosaicism is defined as the embryo having cells with different chromosome make-up. Typically, all cells of the embryo have the same chromosomal make-up as they originate from the same fertilised egg. However, it is possible for cells of the same embryo to have differing numbers of chromosomes. When the cell analysed has a different chromosomal complement than all the others in the embryo a misdiagnosis occurs. Due to the chance of misdiagnosis as well as the presence of aneuploidies, for which testing is not available, we recommend prenatal testing as stated earlier.

SUMMARY OF REASONS TO CONSIDER PGD

- Recurrent miscarriage.
- Over 4 unsuccessful IVF cycles.
- Family history of structural chromosomal condition.
- Advanced Maternal Age.
- Family history of X-linked disease.
- Severe Male Factor Infertility.

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Contact

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