

12.2.12.1 Preimplantation Genetic Testing

Background

Preimplantation genetic testing is used in conjunction with in vitro fertilization (IVF) and allows identification of embryos that are; 1) free of chromosome abnormalities, or 2) free from known genetic disorders. These procedures are known as preimplantation genetic screening (PGS) and preimplantation genetic diagnosis (PGD) respectively. Transferring embryos with the correct number of chromosomes may increase the chance of a successful pregnancy. For couples who are at risk of passing on an inherited condition, only unaffected embryos are chosen for replacement, thus preimplantation genetic testing avoids the need to terminate a pregnancy as may occur when a defect is identified using prenatal testing such as amniocentesis or chorionic villous sampling.

How Does Preimplantation Genetic Testing work?

Preimplantation Genetic testing requires couples to go through routine IVF or intracytoplasmic sperm injection (ICSI) (refer to information sheets 12.3.5; 12.3.8)) so that their embryos can be tested before being transferred to the woman's uterus. Three days after fertilization when the embryos are at the 5 to 8 cell stage of development, one or two of the embryonic cells can be removed by embryo biopsy. The embryo biopsy procedure involves making a fine hole in the zona pellucida (outside shell surrounding the embryo) and gently removing the cell(s). The cells are then processed and tested to see if they have the normal number of chromosomes (PGS), or are free from the genetic condition being tested for (PGD). The embryos that are identified as being normal can then be transferred to the woman's uterus in the hope of establishing a healthy pregnancy.

The embryo biopsy procedure is routinely performed in many centres around the world and does not appear to harm the developing embryo. It has been estimated that biopsy is successful in well over 95% of embryos.

PGS

Testing of the biopsy cells to detect the number of chromosomes is done using a technique called Fluorescent *in situ* Hybridization (FISH). This technique uses fluorescent dyes (or probes) which attach to specific chromosomes within the biopsied cell. Using a specialized microscope allows the chromosomes to be visualized and counted. Probes are now available for a range of chromosomes including numbers 13, 15, 16, 18, 21, 22, X and Y.

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Who might benefit from PGS?

Couples with an increased risk of producing embryos with the incorrect number of chromosomes (aneuploidy) may benefit from PGS. This includes couples who are identified carriers of a chromosome disorder, couples where the female is of advanced age or where the couple has a history of recurrent miscarriage or repeated implantation failure after IVF. The Reproductive Technology Council has approved the following conditions for PGS:

- Women over 35 years of age providing eggs; or
- Women with > 2 miscarriages; or
- Women with > 2 failed IVF attempts where embryos have been transferred; or
- Women referred by a clinical geneticist with a family history of aneuploidy not caused by translocations or other chromosomal rearrangements

PGD

To test for the presence of a specific genetic condition, a technique called polymerase chain reaction (PCR) is used. This technique has the capacity to make millions of copies of the piece of DNA being tested for and therefore allows reliable diagnosis in each of the embryos.

Who might benefit from PGD?

PGD may be beneficial to couples who are at risk of passing on a genetic condition to their children. These include couples with a family history of an inheritable genetic condition, are carriers of a genetic condition or are affected by a genetic condition. Some of the genetic conditions that PGD has been used for include:

- Cystic Fibrosis
- Huntington's disease
- Myotonic Dystrophy
- β -thalassemia
- Spinal Muscular Atrophy
- Fragile X
- Haemophilia

Many other conditions, including rare familial ones may be tested.

If a particular condition has not been tested before, it may be possible to "tailor make" diagnostic tests specifically for families, particularly those with rare genetic conditions.

Specific approval from The Reproductive Technology Council must be sought before couples can proceed with PGD. Approval requires a report from a Clinical Geneticist who has discussed the matter with the participants.

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Considerations

Embryo biopsy procedures have been used extensively in major IVF clinics throughout the world since the early 1990s. Follow up studies have shown that the procedure is safe with no known adverse affects on the embryo's potential to implant and develop normally.

It is important to understand that a genetic diagnosis might not be possible from every embryo. This may result from embryos not being of sufficient quality to biopsy and/or test results not being conclusive for some embryos. In addition, there may be a small risk that an embryo will not survive the biopsy procedure.

For PGS with FISH for chromosome testing usually only one of the developing cells are analyzed. It is possible that the cell being tested will have a different number of chromosomes to other cells of the embryos (mosaicism).

Not all of the total 46 chromosomes are tested and FISH can only detect irregularities of chromosome number for chromosomes 13, 15, 16, 18, 21, 22, X & Y. Although these chromosomes are the most common associated with infertility and miscarriage, some abnormalities in other chromosome are not detected.

In addition, the error rate from FISH may be 6-10%.

Data collected from 62 international PGD centres indicates greater than 97% accuracy with PGD. Even though the diagnostic accuracy of PGD is high, prenatal diagnosis is recommended in an ensuing pregnancy.

Over 700 children world wide have been born following PGD with no increased risk of birth abnormalities reported compared to IVF or ICSI apparent.

If you have any questions regarding PGS / PGD please contact our Scientific Director on 9382 2388.