Preimplantation Genetic Testing (PGT)

Key points:

- PGT involves screening in vitro fertilization (IVF) generated embryos for genetic conditions prior to embryo transfer.
- PGT is available for single gene disorders, translocations, inversions, chromosomal aneuploidy or X-linked disorders.
- Only embryos that are unaffected will be considered suitable for transfer. Embryos that are affected or found to have a chromosome abnormality will not be considered suitable for transfer.
- PGT is NOT 100% accurate. Confirmatory prenatal diagnosis is highly recommended if a pregnancy is achieved following PGT.

What is Preimplantation Genetic Diagnosis/Screening (PGT)?

PGT is a reproductive option for those at risk of passing a specific genetic disease or chromosome imbalance to their children. PGT involves screening IVF generated embryos for genetic conditions prior to embryo transfer, with only unaffected embryos transferred to the uterus. This provides the opportunity to screen embryos for genetic conditions before a pregnancy is established (Figure 1).

Figure 1: Preimplantation Genetic Testing

| IVF | Biopsy (1 or more cells) | Genetic Screening | Unaffected embryos transferred |

Individuals choose PGT over prenatal diagnosis for many reasons including objection to termination of pregnancy, loss of a child from the genetic disease, recurrent implantation failure or recurrent miscarriage.

PGT testing may be appropriate for:

- Individuals at risk of passing a single gene disorder on to their children
- Individuals at risk of having children with a particular X-linked disorder
- Individuals who carry a balanced chromosome rearrangement
- Individuals with an altered sex chromosome complement (eg: XXY)
- Individuals with advanced maternal age (>36 years of age)
- Individuals who have experienced recurrent implantation failure
- Individuals who have experienced recurrent miscarriage
- Individuals who have previously had a pregnancy with a chromosome abnormality

Genetic counselling is an important step to ensure that PGT is the right way forward.
PGT at Monash IVF

Monash IVF has offered PGT since 1994 and is one of the few centres in Australia that specialises in this area of reproductive medicine. Monash IVF Clayton (in Melbourne, Australia) has a highly specialised in-house genetics team, which helps ensure the highest quality of care to patients. The genetics team is responsible for providing a specialised PGT service not only to our own patients but also to patients undergoing IVF cycles at numerous IVF clinics throughout Australia and New Zealand. While the main PGT laboratory is located at Clayton, embryo biopsy can be performed away from the PGT laboratory and the embryonic cells sent by courier to Clayton. Centralising the PGT testing enables patients to access the highest levels of expertise without having to leave their home state. Monash IVF has consistently been at the forefront of PGT technology. Some of our milestones are listed in Figure 2.

Figure 2: Key PGT milestones at Monash IVF

- **1994**
  - PGT for sex selection introduced

- **1996**
  - Monash IVF announces the birth of Australia’s first PGS babies
  - PGT for aneuploidy screening of chromosomes X, Y, 13, 16, 18, 21, 22 introduced

- **1999**
  - PGT for single gene disorders introduced
  - Australia’s first laser zona drilling for embryo biopsy

- **2000**
  - PGT for translocations introduced

- **2004**
  - Aneuploidy screening expanded to include analysis of chromosome 15

- **2009**
  - Aneuploidy screening expanded to include analysis of chromosome 17

- **2010**
  - Monash IVF celebrates the birth of our 300th PGT baby and achieves a further 42 ongoing PGD pregnancies

- **2012**
  - Monash IVF is the first clinic in Australia to introduce SNP-array based PGT technology. This technology represents a significant advance in PGT

- **2013**
  - Monash IVF introduces array-CGH technology as a new PGT technology, enabling aneuploidy screening of all 24 chromosomes and the detection of chromosome imbalances associated with known chromosome rearrangements.

- **2015**
  - Monash IVF introduces Next Generation Sequencing as a new PGT technology, enabling a more comprehensive and higher resolution analysis of the genetic status of IVF embryos.

- **2015**
  - Monash IVF introduces Karyomapping as a new PGT technology, significantly reducing the turn around time for single gene PGT feasibility testing and providing a more cost effective option for patients.
**Fact Sheet**  
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**What does PGT involve?**

Individuals requesting PGT must first undertake an IVF cycle to stimulate the woman's ovaries to produce a number of eggs. These eggs are collected and fertilised using the male partner's sperm. The resulting embryos are cultured in the laboratory (See Figure 3).

Figure 3: Embryo culture

![Embryo culture stages](image)

Embryo biopsy is typically performed on Day 5/6 after egg collection. By this time, the embryo should have developed to the blastocyst stage, and should consist of an inner cell mass (which will go on to form the fetus) and trophectoderm cells (which will go on to form the placenta). Embryos need to have a clear inner cell mass and a suitable number of healthy trophectoderm cells to be considered suitable for biopsy. A small hole is made in the outer shell of the embryo on Day 3 of development and the embryo is returned to the culture dish. By Day 5/6, some of the trophectoderm cells should have herniated through the hole in the outer shell of the embryo and these cells can be collected for analysis. Approximately 5 trophectoderm cells are removed for genetic analysis (Figure 4).

Figure 4: Day 5/6 embryo biopsy

![Embryo biopsy](image)

The biopsied cells are transferred to a small tube for genetic testing. Due to the time taken to perform the genetic testing, the embryos must be frozen following biopsy. It is important that patients are aware that some embryos will not be considered suitable for biopsy, some embryos will not be considered suitable for freezing, and some embryos may not survive the freeze/thaw process. A Genetic Counsellor or Scientist will discuss the PGT results with the patient at the completion of testing.

If an embryo is found to be unaffected and is genetically suitable for transfer, it can be thawed for use in a frozen embryo transfer cycle. The patient's IVF nurse will organize a pregnancy test to be performed on Day 16 of the frozen embryo transfer cycle. Surplus unaffected embryos will remain in storage. These embryos may be used in a subsequent cycle. Embryos that are found to be affected will be removed from storage and allowed to succumb.
Accuracy of diagnosis

The results obtained from PGT are NOT 100% accurate. Test accuracies vary from 90% to 99%, depending on the PGT test used. Consequently, there may be up to a 10% error rate associated with PGT.

Many factors influence the accuracy of PGT testing including:

- The cell/s biopsied from the embryo. It is possible that the biopsied cell/s are NOT representative of the entire embryo. This may lead to a misdiagnosis.
- The clarity of results obtained. Some PGT results are more difficult to interpret than others. If the results are not clear a reduced accuracy may be reported.

Every effort is made to ensure that the PGT test offered has the highest possible accuracy using the currently available technology. However, given that PGT is not 100% accurate, confirmatory prenatal diagnosis is highly recommended.

Other important information

- Embryo biopsy has been performed extensively throughout the world. Follow up studies at Monash IVF have shown that the procedure is safe and does not appear to have an adverse affect on the embryo’s potential to implant and develop normally.
- Not all embryos will be considered suitable for biopsy. Day 5/6 biopsy will only be performed on embryos that have a clear inner cell mass and a suitable number of healthy trophectoderm cells.
- Due to the complexity of the genetic tests, an inconclusive result may be obtained for some or all embryos. In some situations it may be possible to re-biopsy these embryos to try to obtain a conclusive result. If this is possible and unaffected embryos are identified, these may be transferred in a frozen embryo transfer cycle.
- PGT tests are specifically designed to detect genetic abnormalities related to the clinical indication for referral (ie: single gene disorder, translocation, inversion, aneuploidy screening or sex selection). The test does not give any information relating to other genetic conditions or abnormalities.

What are the costs?

Information relating to the cost of PGT is available from your IVF clinic.

How to get started

Those interested in PGT should discuss this procedure with their IVF doctor or with a member of the Genetics team. Genetic counselling may help individuals decide whether PGT is the right option for them.

Individuals considering PGT are encouraged to meet with a clinical geneticist and/or genetic counsellor to discuss the PGT process. During this consultation the genetic specialists will:

- Thoroughly review the genetic history.
- Provide the couple with information regarding the PGT process.
- Answer any questions the couple has in relation to their specific genetic condition and the PGT process.
- Arrange for any further clinical and/or DNA testing to confirm genetic status.
- Arrange for collection of blood samples for test development (if appropriate).
- Offer guidance and support to alleviate any anxiety.

Following counselling, individuals should be aware of the relative risks of embryo screening and the possible outcomes. This will place them in a sound position to make an informed decision about PGT. For further information, please contact our genetic counsellor on +61 03 9590 8357.