

## Fact Sheet

### Preimplantation Genetic Testing for Aneuploidy (PGT-A)



#### Key points:

- Error/s in the early development of the sperm, egg or embryo can lead to an abnormal number of chromosomes in the developing embryos (i.e. missing or extra chromosomes)
- An abnormal chromosome number can cause implantation failure, miscarriage, or the birth of a child with a chromosome abnormality (e.g. Down syndrome).
- Some individuals have an increased risk of producing embryos with an abnormal chromosome number.
- Preimplantation Genetic Testing for Aneuploidy (PGT-A) can be used to screen embryos for abnormalities in chromosome number. Only embryos which are found to be chromosomally normal for the tested chromosomes are considered suitable for transfer.
- PGT-A is NOT 100% accurate. Confirmatory prenatal diagnosis is recommended if a pregnancy is achieved following PGT-A.

### Using Preimplantation Genetic Testing (PGT-A) as an embryo selection tool?

Whenever more than one embryo is obtained from an IVF cycle, a selection process takes place to decide which embryos are the most suitable for transfer or freezing. Current selection criteria include the appearance and the rate of development of the embryos.

Preimplantation genetic testing offers the opportunity to add a further selection criterion, the genetic complement of the embryo, to enhance this selection process and improve the chance of choosing an embryo capable of a healthy live birth.

### What is aneuploidy?

An individual's genetic information is packaged into strings of DNA called chromosomes. Normal embryos contain 46 chromosomes, or 23 chromosome pairs. These chromosome pairs are labelled 1 to 22 (the autosomes) and X and Y (the sex chromosomes). Aneuploidy is when an embryo has the wrong number of chromosomes (i.e. missing or extra chromosome/s) due to errors in cell division in the developing egg, sperm or embryo.

The likelihood that this might happen in an embryo increases as a woman ages (Figure 1). Most aneuploid embryos do not implant and you do not get pregnant. However, some aneuploid embryos can implant but the resulting pregnancy usually miscarries. A small percentage of aneuploid embryos can develop to a baby, the most common of which is trisomy 21, commonly known as Down syndrome.

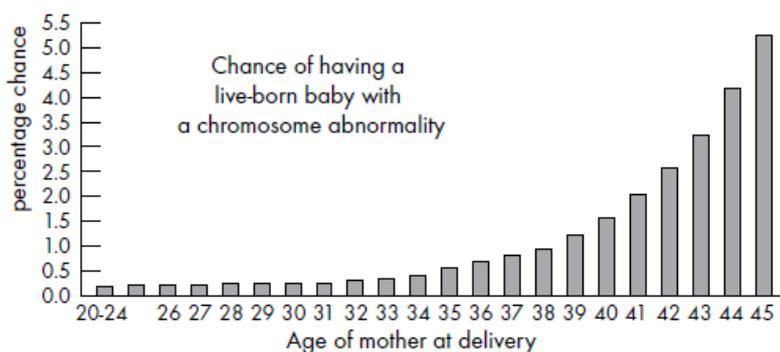


Figure 1: Chance of having a live-born baby with any chromosomal abnormality according to the mother's age at delivery. From The Australian Genetics Resource Book, 8<sup>th</sup> Edition, Centre for Genetics Education, 2007.

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## What is Preimplantation Genetic Testing for Aneuploidy?

Pre-implantation Genetic Testing for Aneuploidy (PGT-A) can be used to screen for aneuploidy involving any chromosome.

This testing may be appropriate for:

- Individuals with advanced maternal age (generally older than 37 years)
- Individuals who have experienced repeated miscarriage
- Individuals who have experienced repeated IVF failure
- Individuals who have previously had a pregnancy with a chromosomal abnormality
- Individuals where one partner has an altered sex chromosome complement (e.g. XXY)
- If embryos of only a specific gender are suitable for transfer, to reduce the risk of a specific genetic condition in a child.

However your fertility specialist can advise further whether PGT-A would benefit your treatment.

Social sex selection (transferring embryos of a specific gender because of parental preference) is not considered ethical under NHMRC\* guidelines in Australia and is therefore not allowed.

## What is involved?

Most embryos created with the intention of undergoing PGT-A are created using a fertilisation method called Intracytoplasmic Sperm Injection (ICSI). ICSI involves the injection of a single sperm into the egg, and is specifically used to minimise any risks associated with the presence of additional sperm around the developing embryo. If standard IVF insemination is performed instead of ICSI, there is a small (unquantifiable) risk that it may have an impact on the ability to obtain a conclusive PGT-A result and/or may reduce the accuracy of the PGT-A result that is obtained. It should also be noted that currently IVF standard insemination cannot be used for NIPGT (see below).

- It is important to note that PGT-A testing can only be performed on embryos that are suitable for freezing. The laboratory will grow embryos in the laboratory until day 6. Any embryo that has not formed a viable blastocyst by day 6 is not suitable for freezing and will not be tested.

For all PGT-A testing the embryos will be frozen while a genetic result is obtained. Some embryos may not survive the freeze/thaw process.

Scientists then need to obtain a sample of the embryo's DNA, which can be done by one of two methods described below. In some cases your doctor may request a combination of both testing. Your doctor will guide you as to the best test for your circumstances.

### 1. Embryo biopsy

Scientists biopsy the developing embryo and transfer the biopsied cells to a small test tube for genetic testing. Due to the time taken to perform the genetic testing, the embryos must be frozen following biopsy.

It is important to note that that

- Embryos need to be at a specific stage of development to be considered suitable for biopsy. Embryos that are too advanced, or less advanced may not be able to be biopsied.
- After embryo biopsy some embryos may be damaged or not develop to a stage suitable for transfer.
- The cell(s) taken at biopsy are assumed to represent the whole embryo however results for other cells within the embryo, but not included in the biopsy sample, may differ.

Final results are usually available 2 weeks after biopsy.

## Fact Sheet

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## 2. Non Invasive PGT – Collecting DNA from the Culture media

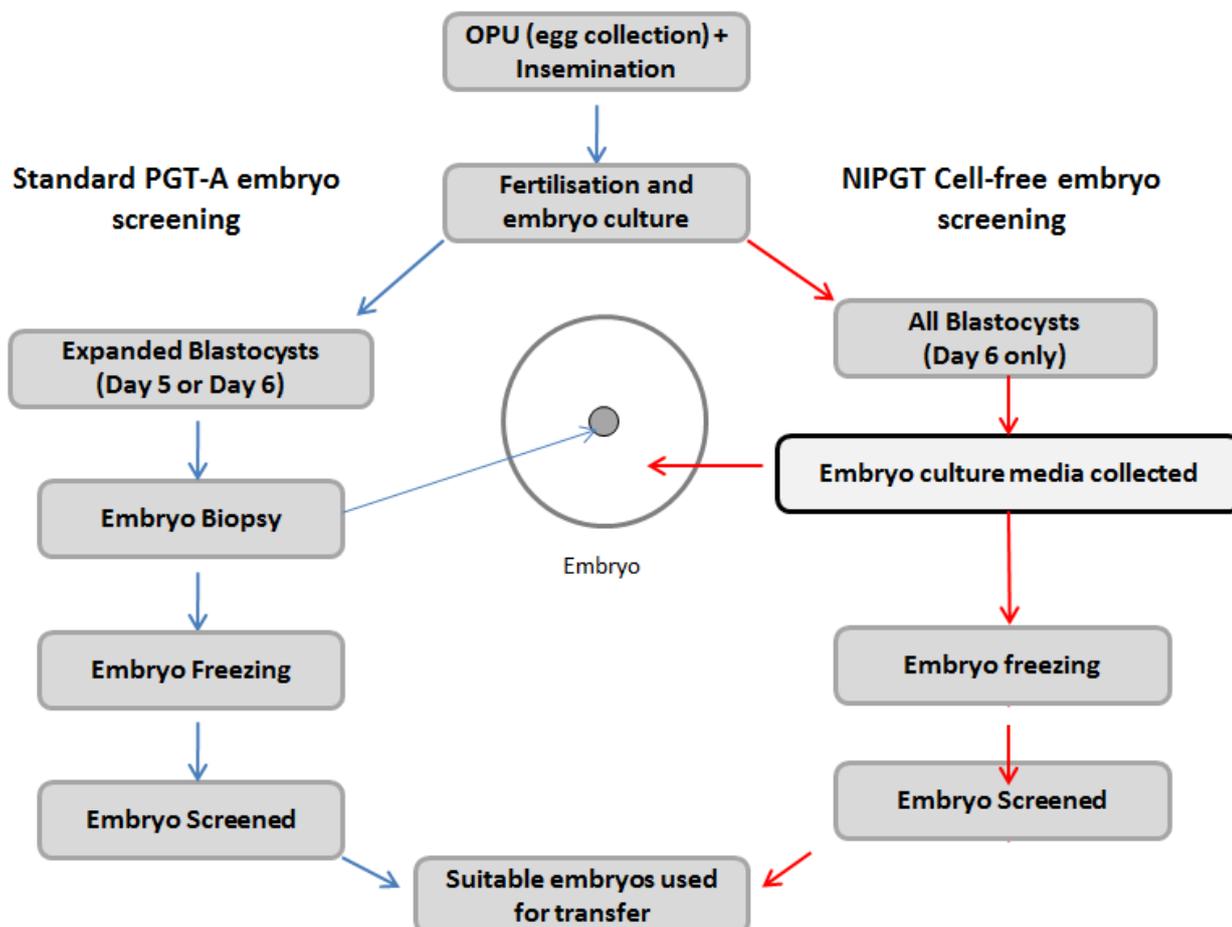
This is a new type of Preimplantation Genetic Testing where scientists take a sample of the leftover nutrient solution (culture media) that the embryo has been growing in while in the laboratory. This solution contains DNA produced by the embryo which can be used for genetic testing. As this procedure can test blastocysts irrespective of stage or quality it can be used for embryos that are not able to be biopsied by day 6.

It is important to note that:

- **This procedure can only be performed on ICSI cycles.**
- Not all embryos release enough DNA for a result to be obtained. **To maximise the chance of having enough DNA to work with, embryos have to be cultured and remain viable until Day 6.** Around 4% of embryos do not secrete enough DNA and will result in a technical failure of the test.
- Our in-house studies have demonstrated that non-invasive PGT results are identical to the embryo biopsy PGT results in 95% of the cases. Therefore, it is important to note that this method is not 100% accurate.

Final results are usually available 2 weeks after sampling.

The figure below demonstrates the differences in DNA sampling methods for the tests.



## Fact Sheet

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#### Results

Whether the DNA is from the biopsy or the culture media, the genetic test to assess the number of chromosomes occurs in the same way. Once a result is obtained your results will be provided to you, and your fertility specialist will also discuss these further at your next appointment.

PGT-A is only designed to analyse chromosome copy number. The test does not give any information relating to other genetic conditions or abnormalities including single gene disorders as well as small duplication/deletions.

There is a 3-5% background population risk for birth defects or genetic conditions in any pregnancy. PGT-A is only designed to detect birth defects caused by aneuploidy and not these other conditions.

	Embryo Biopsy	Non Invasive PGT
Failed Amplification	2.0%	4.7%
No Result	7.0%	4.5%
Accuracy	96.0%	95.0%

#### What are the expected outcomes?

If the test predicts the embryo is very likely to have the right number of chromosomes and is considered genetically suitable for transfer, it can be thawed for use in a frozen embryo transfer cycle.

It is well documented that the frequency of chromosomal aneuploidy increases with maternal age. Therefore, older women will be less likely to obtain a chromosomally normal embryo for transfer compared with younger women. Encouragingly, data indicates that once a chromosomally normal embryo is identified for transfer following PGT-A, the pregnancy rate in older women is not significantly different from that of younger women.

#### Other important information

- Due to the complexity of PGT-A, it may not be possible to obtain a conclusive result for some or all embryos. In this case, the embryo/s can either be thawed and transferred without a genetic result, thawed and re-biopsied if it/they reach an appropriate stage of development, or thawed and allowed to succumb.
- It is possible that at the completion of the cycle there will be no embryos available for transfer. This may occur as a result of one of the following scenarios:
  - All embryo samples tested during an IVF cycle may be found to be aneuploid, meaning that no embryos are genetically suitable for transfer.
  - Embryos diagnosed as chromosomally normal may not survive the freeze/thaw process and therefore may not be suitable for transfer.
  - Embryos diagnosed as chromosomally normal may survive the freeze/thaw process, but may not continue to develop normally and therefore may not be suitable for transfer.
- There are some rare chromosomal problems that cannot be tested for using PGT-A.
- This test is only a screening test and therefore cannot provide an absolute guarantee of the chromosome status of the embryo. In some embryos, the biopsied cell/s or culture media may not be representative of the whole embryo.

While every effort is made to ensure that the PGT-A test offered has the highest possible accuracy using the currently available technology, results are not 100% accurate. **Therefore, prenatal diagnosis is highly recommended in an ensuing pregnancy.**

#### What are the costs?

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