

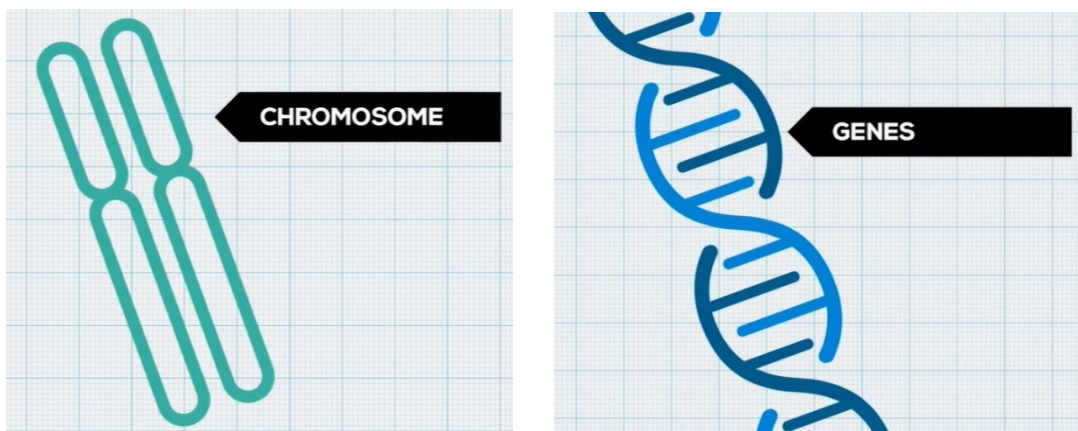
PGT-A

Preimplantation Genetic
Testing for Aneuploidies

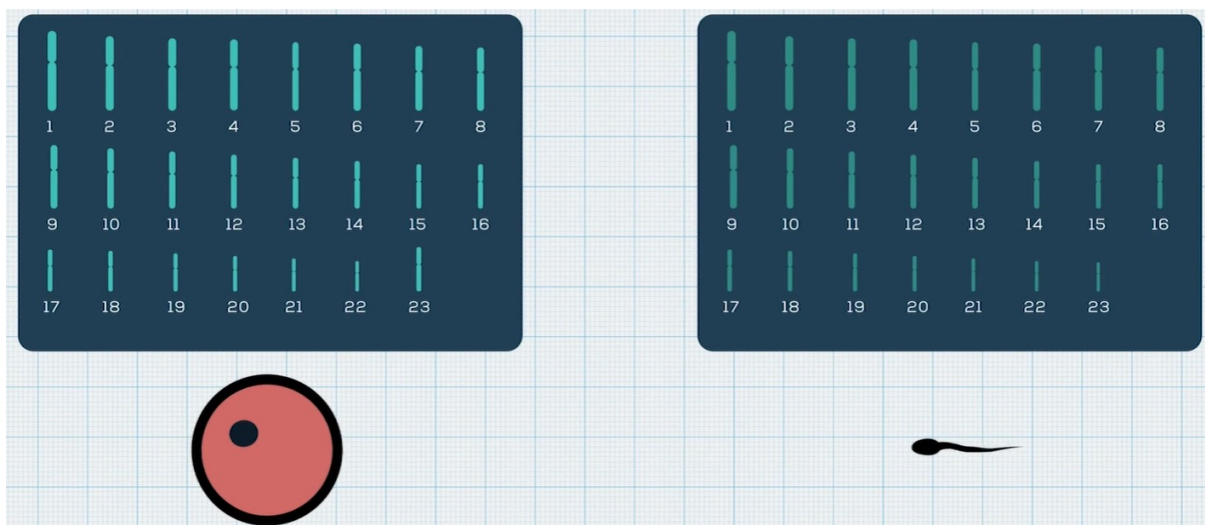
Introduction

Preimplantation Genetic Testing for Aneuploidies also known as PGT-A is a genetic test performed on embryos produced through IVF, or in vitro fertilisation. PGT-A provides information about embryo genetic health to help select the best embryo for transfer and improve your chance of achieving a successful pregnancy.

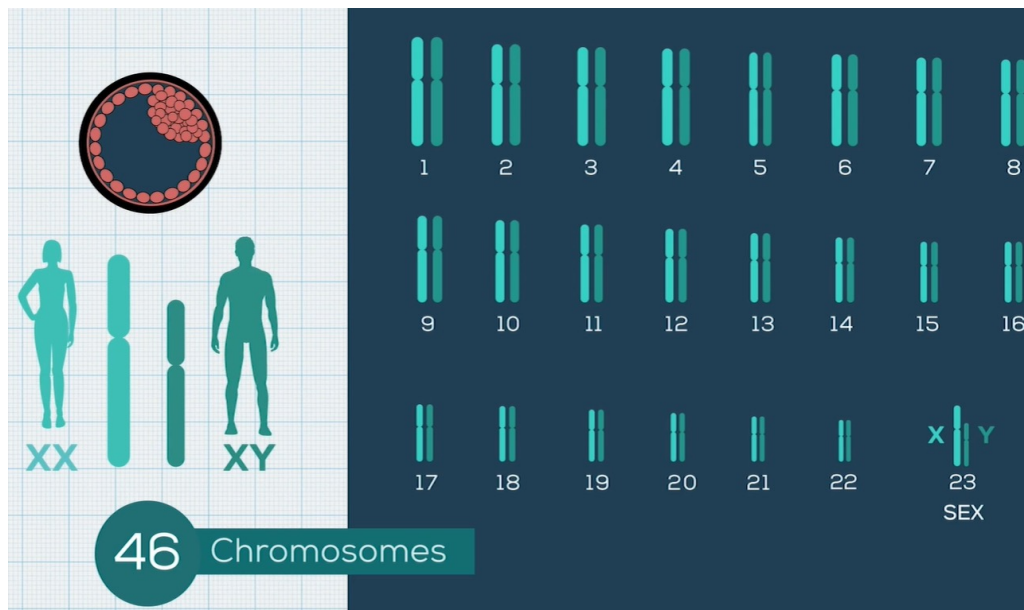
It is helpful to first understand some background information about chromosomes which are structures that carry genetic information in the form of genes.



Egg and sperm cells typically contain 23 single chromosomes each. When a sperm fertilises an egg, the resulting embryo has 23 pairs or 46 total chromosomes. Half of the chromosomes in the embryo are inherited from the egg and half are inherited from the sperm.

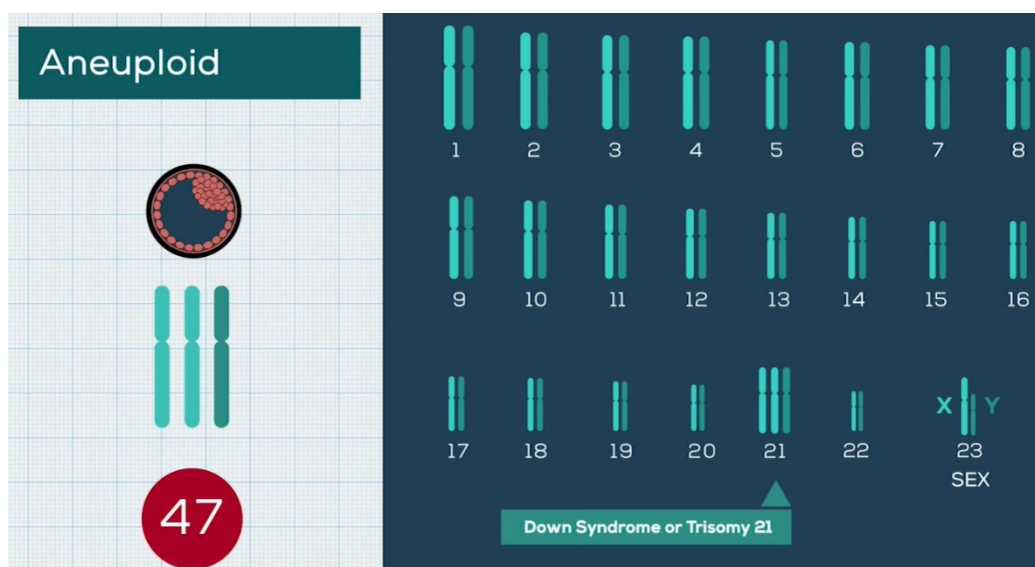


The sex chromosomes, X and Y, determine one's sex. XX for female and XY for male.



If an embryo doesn't have the right number of chromosomes, it can result in a failure to conceive, miscarriage, stillbirth or a child born with disabilities. These embryos are known as aneuploid embryos.

A common example of aneuploidy is Down Syndrome (Trisomy 21) which is caused by having three copies of chromosome 21, instead of two. Another common example of aneuploidy is Turner Syndrome (Monosomy X) which is caused by having only one copy of the X chromosome, instead of the usual two sex chromosomes.



Merrion Fertility Clinic will only recommend PGT-A for a patient or couple with a medical indication that may benefit from PGT.

The clinical criteria for this are

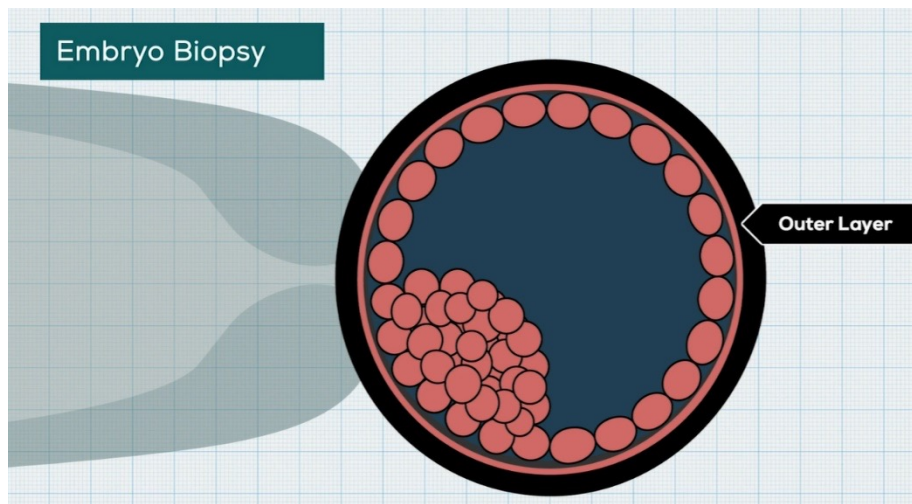
- Female age > 35 years in patients planning fresh IVF/ICSI.
- Recurring Implantation failure
- Recurring miscarriage which is likely due to chromosomal aneuploidy.

PGT may be considered in the management of patients who have a large number of embryos in cryostorage.

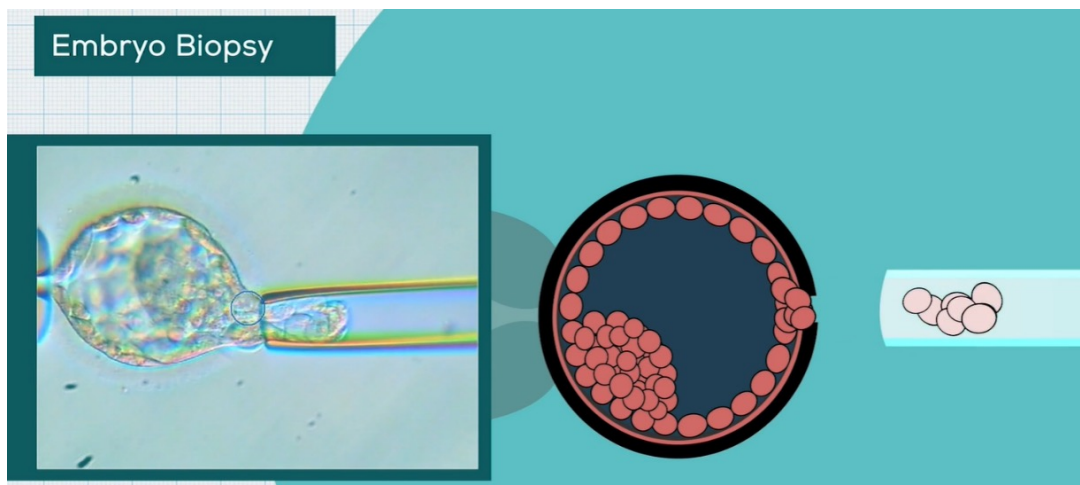
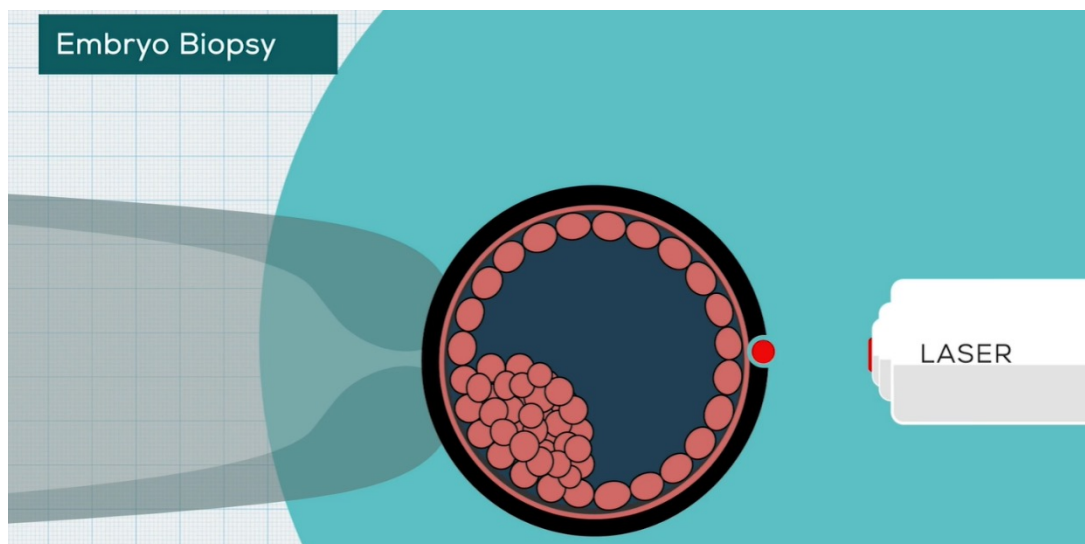
Through PGT-A, it is possible to test a sample through each individual embryo, to determine if it has the correct number of chromosomes. This process helps your team to help you decide which embryo to transfer. As chromosomally normal embryos are the most likely to develop to term and lead to a healthy baby, PGT-A can help some women or couples to increase their chance of a successful pregnancy.

Embryo Biopsy

In order to perform PGT-A, a small number of cells are removed from the embryo via a biopsy and the sample is sent to a specialised genetics laboratory for analysis. The lab Merrion Fertility Clinic use is Cooper Genomics, which is based in the UK. Embryos are typically biopsied on day 5, day 6 or day 7 after egg retrieval. Only embryos with satisfactory quality that continue developing to this stage are tested. By this time the embryo contains over 100 cells and several cells can be removed from the outer layer of the embryo, which is the part of the embryo that will eventually become the placenta.



In order to most effectively remove these cells without damaging the embryo, a highly skilled embryologist will make a small hole in the shell of the embryo and use an instrument that is less than 1/10th the diameter of a human hair to carefully perform the biopsy.



The cells obtained from the biopsy are then washed to remove any potential sources of contamination and transferred into small tubes and sent to the CooperGenomics laboratory for analysis. Only the biopsy sample is sent off site. The embryos remain at Merrion Fertility Clinic and are cryopreserved by until the PGT-A results are returned.

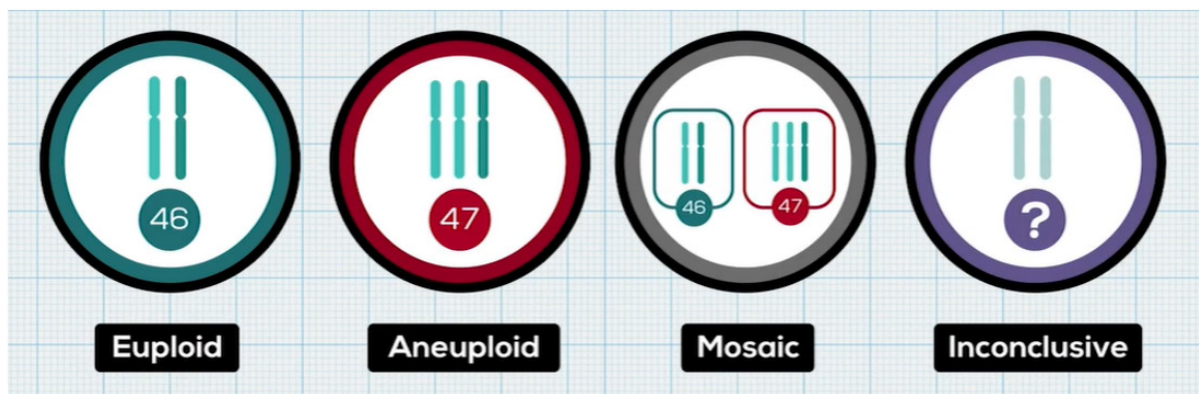
Thus far, babies born after procedures that include embryo biopsy have not had an increased rate of birth defects. Although data has shown that embryo biopsy has no adverse impact on growth or medical outcomes, there is potential for unknown consequences to live born babies.

An embryo may be damaged during biopsy, which will cause it to not be suitable for transfer. With a skilled embryologist, the risk of damaging an embryo is very low. While it is important to understand the risks involved in the process, embryos have been biopsied for over 25 years and have resulted in tens of thousands of healthy pregnancies.

PGT-A Analysis

Once the biopsied cells arrive at the genetic testing laboratory, PGT-A is performed to determine the number of chromosomes in each embryo sample. The report from the laboratory will indicate whether or not the embryos have the normal number of chromosomes, giving the clinical team information to help you make an informed decision about transfer.

The embryos may be Euploid, Aneuploid, Mosaic or inconclusive.



Euploid

The embryo sample has the normal number of chromosomes. Embryos with a euploid PGT-A result have been shown to have higher implantation rates, lower miscarriage rates and higher live birth rates.

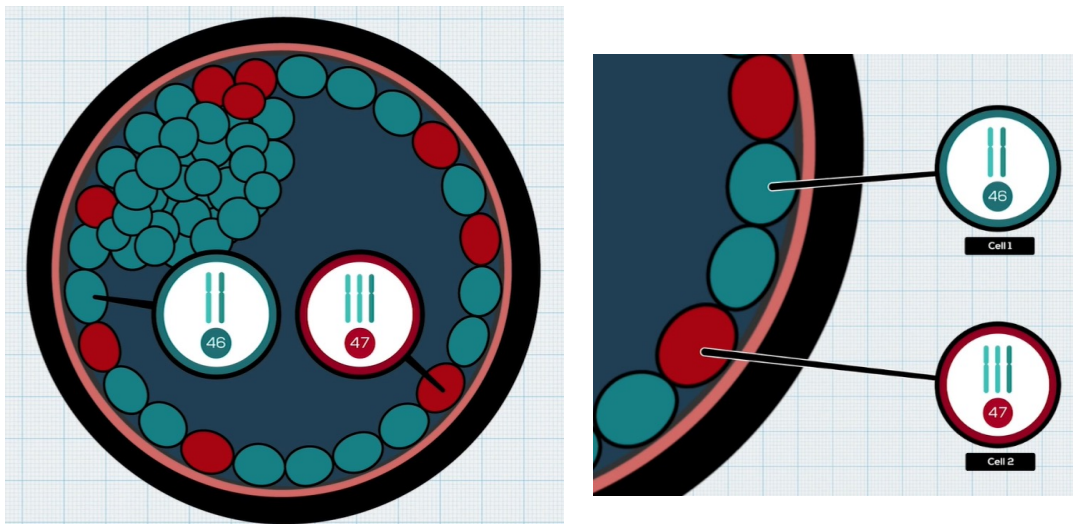
Aneuploid

The embryo sample has an extra or missing copy of a whole or part of a chromosome. Embryos with an aneuploid PGT-A result may lead to implantation failure, miscarriage, stillbirth or a child born with disabilities.

Mosaic

Some cells in the embryo sample have the normal number of chromosomes and some cells have an abnormal number of chromosomes. These embryos have a lower rate of implantation and higher rate of miscarriage than euploid embryos, but they can lead to live births.

Mosaicism is the presence of two or more different cell types within a single tissue, individual, or in this case, embryo.



A mosaic PGT-A result means that some cells in the biopsied sample have the normal number of chromosomes and some cells have an abnormal number of chromosomes. It's estimated that approximately 20% of PGT-A tested embryos are mosaic.

Mosaicism in embryos has always existed, but it has only become detectable by PGT-A in the last several years due to advancements in technology. Before that, mosaic samples were being classified as either euploid or aneuploid. Because the ability to detect mosaic results is relatively new, it is important to note that mosaicism follow-up data is limited. The research performed to date is preliminary and based on small sample sizes.

Based on the data currently available, mosaic embryos have been shown to have a lower rate of implantation and higher rate of miscarriage than euploid embryos. But they can lead to live births.

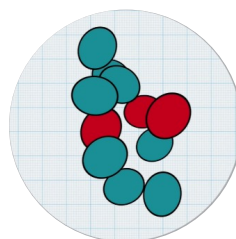
If ONLY mosaic embryos are available, options to consider include:

- Pursuing another IVF + PGT-A cycle with the goal of identifying a euploid embryo
- Or, consider the risks and benefits of transferring a mosaic embryo, including which specific chromosome is involved and the level of mosaicism in the sample.

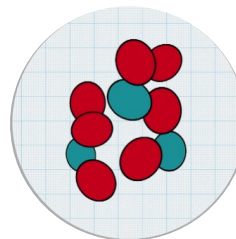
In a mosaic embryo sample, the level of mosaicism is the ratio of normal cells to abnormal cells. This proportion is thought to be associated with the chance of success.

- Low level mosaics have few abnormal cells and are thought to have a higher chance of IVF success.
- High level mosaics have more abnormal cells and are thought to have a lower chance of IVF success.

**Low Level
Mosaicism**



**High Level
Mosaicism**



Inconclusive

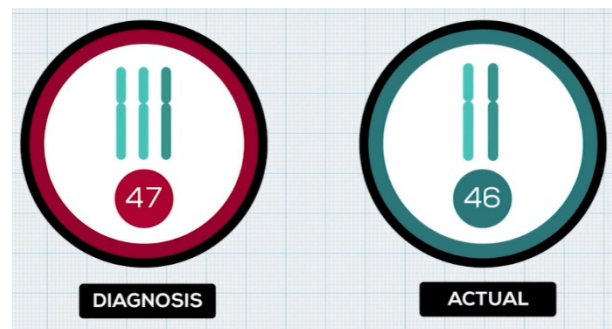
This means that the testing could not be performed to identify the chromosomal complement of the embryo. Inconclusive results occur in about 2% of cases.

It's important to remember that PGT-A is being performed on a small sample of cells from the embryo, not the entire embryo. While PGT-A accuracy rates are greater than 97%, there is always a chance that the cells sampled may not be representative of the entire embryo.

There is a small chance of misdiagnosis due to the limitations of the test, either by false positive or false negative.

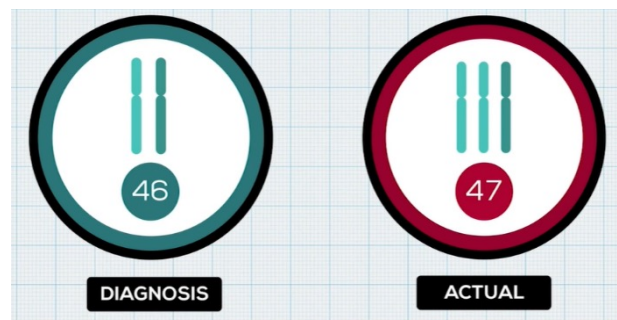
False Positive

This means that an embryo is diagnosed as chromosomally abnormal when it is in fact normal.



False Negative

This means that an embryo is diagnosed as normal when it is in fact chromosomally abnormal.



In extremely rare cases, human error or natural forces beyond the control of Merrion Fertility Clinic or the genetic testing centre, such as weather and air travel issues, can result in an inability to perform testing and receive results.

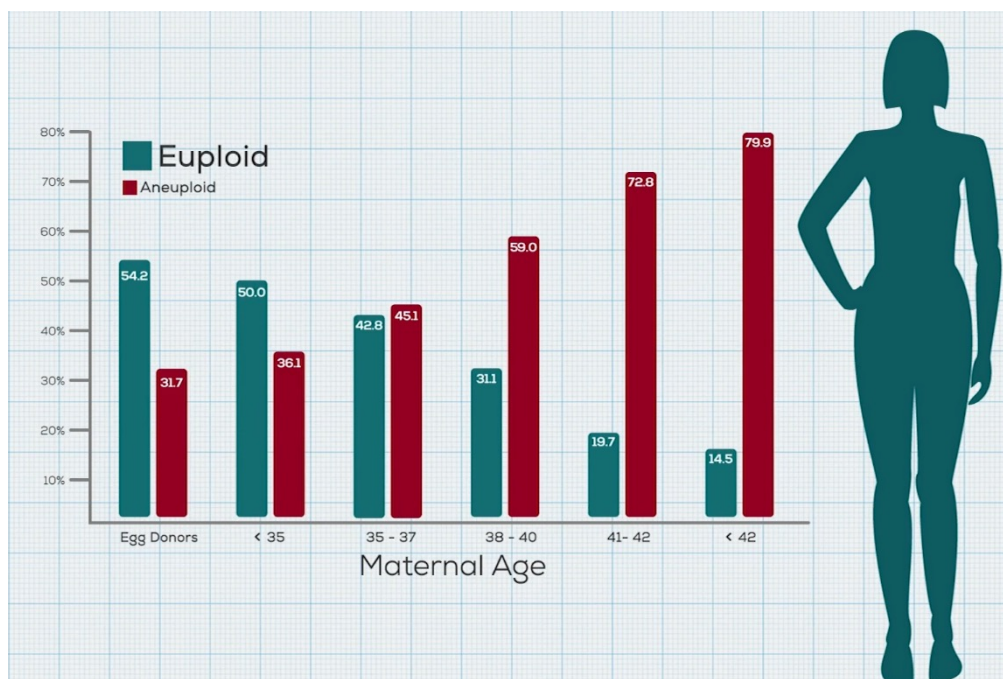
Remember, even in this rare scenario, only the sample that was biopsied is impacted. Your embryos will still be safe at Merrion Fertility Clinic.

Lastly, sexual intercourse during IVF treatment may result in a spontaneous pregnancy. Sperm from intercourse may result in fertilisation and implantation in addition to, or instead of, fertilisation and implantation from IVF. This would invalidate the results from PGT. Please consult with the Merrion Fertility Clinic team about timing of sexual intercourse during your IVF treatment.

Embryo Transfer

In most IVF cycles in which PGT-A is performed, the embryos are biopsied and frozen on day 5, 6 or 7. After PGT-A results are received, if there is an embryo available for transfer, a frozen embryo transfer can be performed in a future cycle. The percentage of chromosomally normal embryos can vary widely in any given cycle.

As a woman ages, the likelihood that an embryo will be identified as abnormal increases and the expected number of chromosomally normal embryos available for transfer decreases.



For women at any age, it is possible that there will be no embryos available for biopsy. Or if there are, that no biopsied embryos will be identified as chromosomally normal in a given cycle, meaning that there will be no embryos available for transfer from that cycle. The benefit of PGT-A is that by knowing whether an embryo is chromosomally normal or not, you can avoid transferring an abnormal embryo. With the information provided by PGT-A, it is recommended that a single embryo is transferred as the pregnancy rate per transfer is increased and the miscarriage rate is decreased. With PGT-A, the risk of an ongoing pregnancy having a chromosomal problem is significantly reduced.

PGT-A cannot guarantee the birth of a chromosomally or genetically normal child and is not a replacement for prenatal testing. In fact, prenatal testing should be considered for all pregnancies resulting from IVF with PGT-A. It's important to understand the benefits, risks and alternative options, in order to make an informed decision about pursuing PGT-A. While there is some risk involved, technological advances have made PGT-A an effective tool for improving IVF success rates.

Our Clinic policy on transferring embryos is as follows:

- Euploid – these embryos are recommended for transfer.
- Mosaic – these embryos may be transferred. The patient will discuss the results with their Consultant and will also be required to have a counselling session with a Genetic Counsellor. Based on this, the patient will decide whether to transfer a mosaic embryo.
- Aneuploid – our Clinic policy is not to transfer aneuploid embryos.

PGT-A Limitations

PGT-A cannot guarantee the birth of a chromosomally or genetically normal child and is not a replacement for prenatal testing. In fact, prenatal testing should be considered for all pregnancies resulting from PGT-A. PGT involves biopsying and testing cells taken from the trophoctoderm (the cells that will become the placenta) and not the inner cell mass (the cluster of cells that will become the fetus). Therefore, it is possible that the genetic profile of the cells tested may vary from the cells that will form the fetus.

It's important to understand the benefits, risks, and alternative options, in order to make an informed decision about pursuing PGT-A. While there is some risk involved, technological advances have made PGT-A an effective tool for improving IVF success rates.

In extremely rare cases, human error, or natural forces beyond the control of Merrion Fertility Clinic or Cooper Genomics, such as weather and air travel issues, can result in an inability to perform testing and receive results. Remember, even in this rare scenario, only the sample that was biopsied is impacted. Your embryos will still be safe at Merrion Fertility Clinic.

Lastly, sexual intercourse during treatment may result in a spontaneous pregnancy. Sperm from intercourse may result in fertilisation and implantation in addition to, or instead of, fertilisation and implantation from treatment. This would invalidate the results from PGT. Please consult with the Merrion Fertility Clinic team about timing of sexual intercourse during your treatment.

For more information about PGT-A, please contact Merrion Fertility Clinic.