Embryo testing with PGT-M / PGT-SR

Patient Information

Background

Preimplantation Genetic Testing for Monogenic/Single Gene Defects (PGT-M) or structural rearrangements in Chromosomes (PGT-SR) are genetic tests that can be performed on embryos before they are implanted into the uterus during in vitro fertilization (IVF). The test is used to identify embryos that carry a specific genetic disorder or disease, e.g. cystic fibrosis, sickle cell anemia, or Tay-Sachs disease (PGT-M) or embryos that carry a rearrangement in chromosomes (PGT-SR).

The test is performed on embryos that have been created through IVF or ICSI, by removing a small number of cells from the embryo and analysing the DNA. This process is called preimplantation genetic testing (PGT). Embryos that do not carry the genetic disorder or chromosome rearrangement will be selected for implantation.

Who is it for?

PGT-M is appropriate for people who are at high-risk of passing on a specific single gene disorder. You may consider PGT-M if:

- You and your partner are carriers of the same autosomal recessive condition (e.g. Cystic fibrosis)
- You are a carrier of an X-linked condition (e.g. Duchenne Muscular Dystrophy)
- You or your partner have an autosomal dominant condition (e.g. Huntington disease)
- You or your partner have a mutation associated with a hereditary cancer syndrome (e.g. BRCA1 & 2)
- You had a child or pregnancy with a single gene disorder
- You want to perform HLA matching

It is possible to use PGT-M to test for almost any genetic condition where a specific gene is known to cause that condition. Which conditions can be tested for is regulated by the Human Fertility and Embryology Authority (HFEA). The ability to test for a condition will depend on the seriousness of symptoms and the likely hood of transmission. A full list of conditions which can be tested for is available at **https://www.hfea.gov.uk/treatments/embryo-testing-and-treatments-for-disease/approved-pgt-m-and-ptt-conditions/**. If your condition has not been approved for testing it is possible to apply to the HFEA for a licence, however there is no guarantee of this being approved.

PGT-SR is appropriate for people who have a chromosome rearrangement, and therefore are at risk of creating embryos with the incorrect chromosome number or structure, which are less likely to result in a healthy livebirth. You may consider PGT-SR for chromosome rearrangements if you had a child or pregnancy with a chromosome rearrangement and you or your partner are a carrier of an:

- Inversion
- Reciprocal translocation
- Robertsonian translocation

Prior to embarking on PGT-M / SR you will have met with a genetic counsellor who will have explained the symptoms and impact the condition may have on a child and the risk of passing it on to a child. You will go through a detailed consent process with the genetics team and they will require cheek (buccal) swabs from you both, this is to help develop the test specifically for you. It may also be necessary to ask family members to provide genetic samples. Embryos are created using IVF / ICSI, this process will be explained in more detail by your fertility consultant. Once the embryos have reached the advanced (day 5 or 6) embryo stage (also known as the blastocyst stage), a small sample of cells are removed from the outside of the embryo, known as the trophoectoderm, using a microscopic laser.

These cells are known as 'extra-embryonic' and produce tissues such as the placenta. There are over 100 trophectoderm cells in a blastocyst so the removal of very few of these cells rarely impacts on the embryo. The cells are sent for genetic analysis at a genetics laboratory for the genetic testing. Meanwhile the blastocysts will be frozen, whilst the results of the genetic screening are awaited, this means that there will be no fresh embryo transfer in this cycle. The results take a minimum of 2-3 weeks to come back from the point of biopsy. Unfortunately due to the time and expertise involved in biopsy it is not always possible to biopsy the blastocyst fresh. It may therefore be necessary to freeze the blastocyst and schedule thaw, biopsy and re-freeze on another day.

Our embryology team will inform you at the time of egg collection when your embryo biopsy will most likely occur. Depending on the timing of the biopsy a consultation will be arranged for you with your fertility consultant to discuss the embryo screening results. If the results indicate that there is at least one unaffected embryo, a Frozen Embryo Transfer (FET) will be arranged. This will either be in a natural or programmed cycle and your

consultant will discuss which might be best for you. The remaining embryos unaffected embryos will remain in frozen storage for future use if you wish. One transfer is included in the PGT package, there is an additional cost for subsequent FET cycles. It is important to be mindful that embryos have to be of a certain quality in order to survive the biopsy, freeze and thaw. It may be therefore, that not all of your embryos are suitable for biopsy. Your embryologist will discuss with you on D5 which embryos will be suitable for testing.

It is also possible to test embryos which have already been frozen by thawing them and undertaking the biopsy. The embryo will then need to be re-frozen. There is no evidence to suggest that thawing / re-freezing has a detrimental effect on the embryo although there is always a very small risk of the embryo not surviving a freeze / thaw cycle (approximately 3%). It is only possible to biopsy embryos of a certain quality, it may be that not all the embryos you have in storage are suitable for biopsy, our embryology team will be able to advise which of your embryo(s) is suitable for biopsy.

If there are no embryos suitable for transfer you will be informed of this at consultation and the future treatment options for you will be discussed. Legally we also need your consent to allow the affected embryos to perish. This is included in the PGT consent form but we will confirm with you that you give your consent for this to happen.

What are the risks of PGT-M / PGT-SR?

- **No embryos for biopsy**. There is a chance that no embryos develop on to the blastocyst stage and therefore that there are no embryos for biopsy and transfer.
- **Embryo damage**. There is a risk of embryos being damaged during the biopsy process meaning they are not suitable for freezing and transfer. This risk is very small (approximately 2%).
- **No unaffected embryos**. There is a chance that all the embryos biopsied are affected and therefore that there is no embryo suitable for transfer. The likelihood of this happening will depend on which condition you are undergoing the testing for.
- **Risk of misdiagnosis**. Unfortunately tests are rarely 100% accurate and there is a risk of a an unaffected embryo being incorrectly diagnosed as affected and an affected embryo being diagnosed as being unaffected. The chances of this are less than 2%.
- **Risk of no diagnosis/partial diagnosis**. Some embryos may have no diagnosis, due to the absence of insufficient genetic material in the sample, or technical difficulties in the fixation process the risk of this is up to 3%. In this situation there is the option of retesting the embryo.
- Unfortunately PGT-M / SR does not guarantee a pregnancy or a healthy live birth nor does it eliminate the risk of miscarriage as these things are multifactorial.

Can PGT-A be undertaken with PGT-M / SR?

Yes it can. Standard PGT-M / SR involves testing the embryo for single gene disorders or specific chromosomal rearrangements. It doesn't test the number of chromosomes an embryo carries. PGT-A (also known as Pre-implantation Genetic Screening (PGS)) is a method of screening embryos for chromosomal abnormalities prior to transfer back to the womb at the time of IVF. We know that chromosomally normal embryos are more likely to result in a successful pregnancy and livebirth. PGT-A is a selection tool to increase the likelihood of a healthy on-going pregnancy and is not a guarantee of pregnancy. Couples undergoing PGT-M testing can also elect have their embryos tested for Chromosomal abnormalities with PGT-A. We would recommend you read our separate patient information leaflet on PGT-A testing before making a decision on this.

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