Preimplantation Genetic Testing

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What is Preimplantation Genetic Testing?

Preimplantation Genetic Testing, known as PGT, is a technique used to identify genetic defects in embryos created through *in vitro* fertilisation, IVF, before pregnancy. Some individuals may be at risk of passing on an inherited disorder to their children because they have - or are a carrier of - a genetic disorder. This means a child born may have or carry the disorder.

History of Preimplantation Genetic Testing

PGT was pioneered by an American Embryologist and Geneticist in 1989 to test for the presence of the gene defects that cause Cystic Fibrosis. The biopsy procedure was performed 3 days after fertilisation and resulted in the transfer of an embryo that was negative for the Cystic Fibrosis gene defect. This resulted in the live birth of a baby free of Cystic Fibrosis and was not a carrier of the gene defect. This marked an important development for families who are affected by genetic mutations. Since then PGT has markedly advanced and is used worldwide to create babies free of inherited genetic disorders. A summarised timeline of key events in the development of PGT is presented in *figure 1*.

Figure 1: *Timeline of developments in PGT*

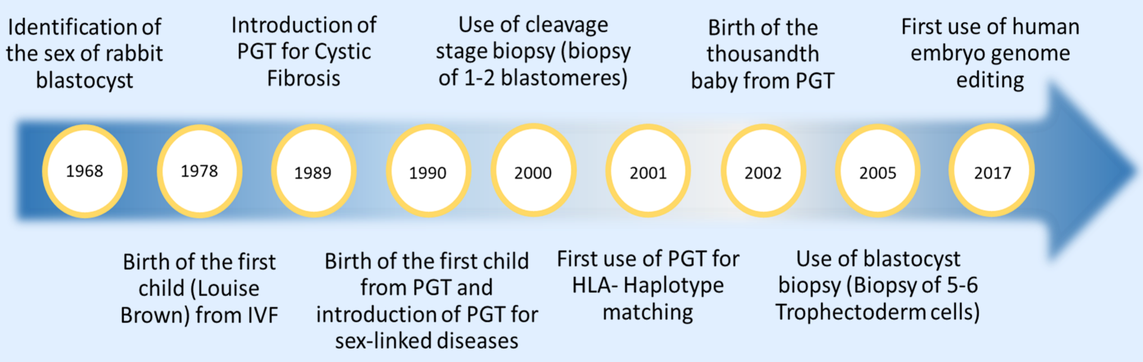
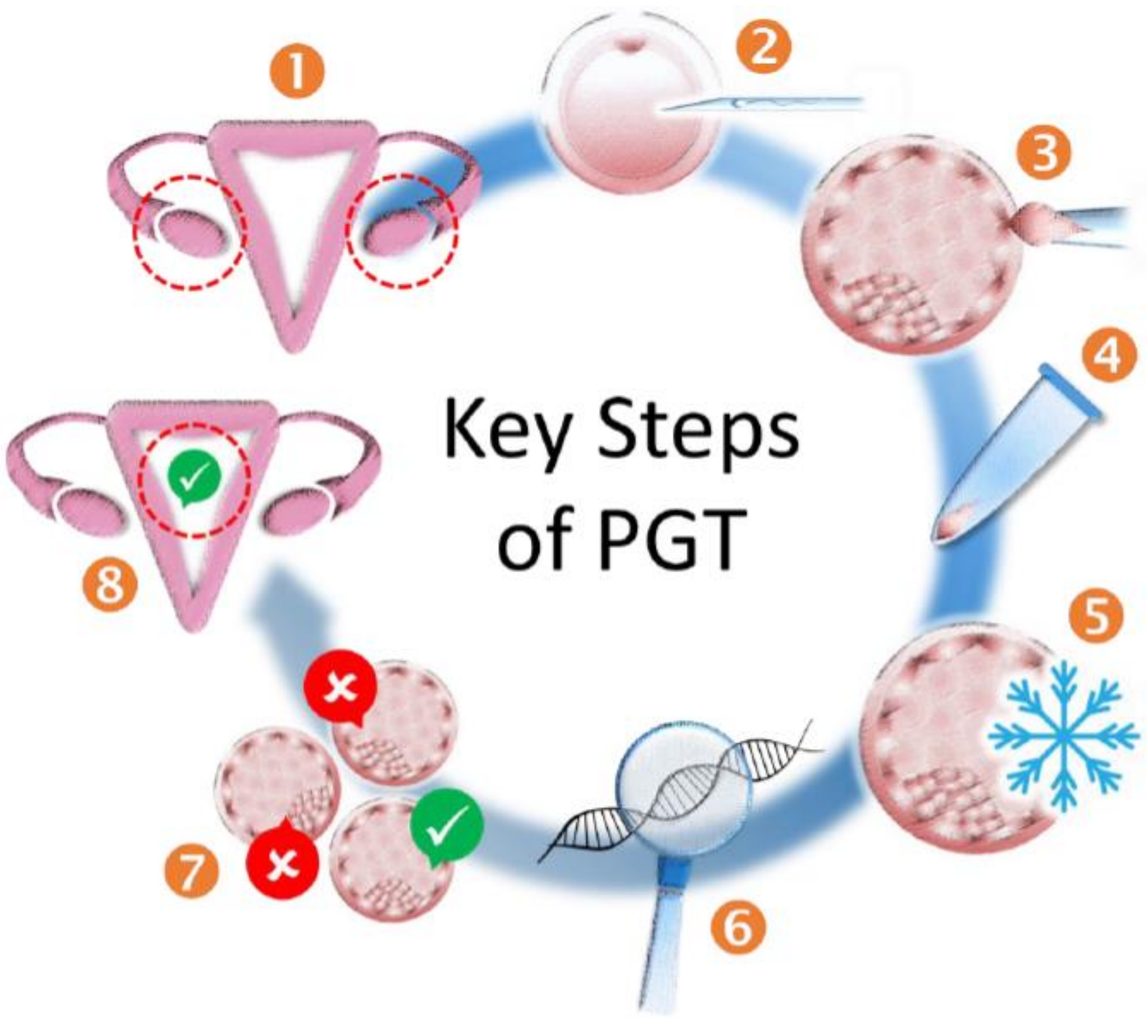


Figure 2: *Key Steps of PGT*



1. Ovarian stimulation and oocyte collection
2. Intracytoplasmic sperm injection
3. Trophectoderm cell biopsy on day 5/6 of embryo development (blastocyst stage)
4. Tubing of biopsied cells which are frozen and sent for genetic analysis
5. Freezing of embryo immediately post biopsy
6. Genetic analysis
7. Evaluation of results and selection of embryos suitable for transfer
8. Transfer of suitable embryo to the uterus

How does Preimplantation Genetic Testing work?

The process of PGT is summarised in *figure 2*. Firstly, the female undergoes ovarian stimulation to produce a cohort of eggs which are fertilised by sperm from the male partner using intracytoplasmic sperm injection. Five to six days after fertilisation the embryos are at the blastocyst stage where the embryo contains two distinct cell types – the inner cell mass, which becomes the baby, and the trophectoderm cells, which become the placenta. Cells from the trophectoderm are removed in the biopsy procedure and sent to the genetic laboratory for identification of the specific disorder the embryos are at a risk of inheriting. The embryos are then frozen whilst awaiting the genetic results. Once the results are returned, the embryos containing the specific disorder can be identified and only embryos which do not have the disorder are replaced back into the uterus of the female in a frozen embryo transfer procedure in the hopes that a pregnancy of an unaffected baby will occur.

How does Preimplantation Genetic Testing help our patients?

PGT allows people who have a serious inheritable genetic disorder the chance at having a child who is unaffected by the genetic disorder. There are three main genetic testing techniques utilised in IVF clinics today.

PGT-M

Tests for *monogenic disorders* which are disorders caused by a single gene e.g. Cystic Fibrosis. This type of testing is most commonly used by individuals who are carriers of a gene disorder; have a known, confirmed gene disorder or have a child who has the gene disorder.

PGT-SR

Tests for *structural rearrangements* of chromosomes. This type of testing is most commonly used by individuals who have, or are carriers of a balanced chromosomal rearrangement which is when sections of two chromosomes have switched place. This testing method is carried out three days post fertilisation.

PGT-A

Tests for *aneuploidy* (abnormalities in chromosome number) in embryos. Aneuploidy can cause embryos to have less chance of developing into a baby, or a baby being born with a genetic condition. This type of testing is most commonly used in women over the age of 37 years old, who have had several miscarriages or failed IVF cycles, people with a family history of chromosome problems, and men whose sperm may carry abnormal chromosomes.

Can everyone have Preimplantation Genetic Testing?

PGT is mostly used for individuals with a known genetic disorder as the technique has associated ethical considerations. Although the procedure can prevent later pregnancy termination, issues have been raised with PGT such as sex selection, which is approved in some countries but prohibited in the UK. There is also debate about the use of PGT in the selection against certain disabilities. The use of PGT in the UK is closely monitored by the HFEA (the Human Fertilisation and Embryology Authority who regulate and oversee all IVF procedures in the UK) who take into consideration specific genetic diseases and the seriousness of the condition before making recommendations as to whether the procedure can be approved. Currently, the HFEA classify PGT-A as having no evidence of improving a patient's chance in having a baby. Therefore, PGT-A is restricted to use with specific patient groups. In addition, patients having all types of PGT are extensively counselled on the risks associated with the procedure to allow them to make an informed choice.

References

1. Human Fertilisation and Embryology Authority (2021).*Pre-Implantation Testing for Monogenic disorder (PGT-M) and Pre-Implantation Testing for Structural Rearrangements (PGT-SR).*