Preimplantation Genetic Diagnosis (PGD) is the genetic testing of embryos, sometimes used in assisted reproductive treatment to reduce the risk or avoid transmission of a genetic disease or chromosomal abnormality. It is a highly sophisticated scientific technique used to select embryos free of genetic disease or abnormalities before the transfer of the embryos back to the uterus.

The aim of PGD is to maximise the chance of a couple having a successful pregnancy and a healthy child.
What is Preimplantation Genetic Diagnosis (PGD)?

PGD is largely used as a means for reducing the risk of an individual or couple passing on a specific genetic or chromosomal disease or abnormality to their child.

In PGD, embryos are generated through the process of IVF and then one or more cells from the embryo are screened for a genetic condition prior to the transfer of the embryo into a woman's uterus.

The screening gives information regarding the genetic status of the embryo, enabling selection of unaffected embryos prior to implantation and before pregnancy is established.

This allows the individual or couple to choose not to be impregnated with an affected embryo, rather than face a difficult choice of whether or not to terminate a pregnancy.

Assisted reproductive treatment clinics in Victoria perform PGD to reduce the risk of or avoid a range of conditions each year.

A list of conditions that PGD is commonly used to identify can be found at [www.varta.org.au/preimplantation-genetic-diagnosis/](http://www.varta.org.au/preimplantation-genetic-diagnosis/).

What are the reasons for having PGD?

PGD is performed for three main reasons:

- When a couple is at risk of having a child with a genetic disorder.

- When one partner of a couple has a chromosome translocation.

- Screening for chromosome abnormalities. PGD may also be appropriate for women from their late thirties or for individuals or couples who have experienced repeated miscarriage or repeated IVF failure.

PGD for sex selection is not legal in Australia unless it is to identify a specific genetic condition affecting one gender.
What is Preimplantation Genetic Diagnosis?

When a couple is at risk of having a child with a genetic disorder

This type of PGD is used as an alternative to prenatal diagnosis (also referred to as chorionic villus sampling or amniocentesis) when a couple have a high risk (typically 25% or 50%) of having a child with a serious genetic disorder. A PGD test can be designed for virtually any genetic disorder, as long as the specific gene fault in the family is known.

Examples of genetic disorders for which PGD is commonly performed are Cystic Fibrosis (CF), Fragile X Syndrome, Huntington Disease and Muscular Dystrophy (MD). Many couples who use this type of PGD do so because they wish to avoid termination of pregnancy.

When one partner of a couple has a chromosome translocation

Chromosomes are the packages of genes that are present in all cells of the body. Normal individuals contain 46 chromosomes, which are arranged in 23 chromosome pairs. These chromosome pairs are labelled 1 to 22 (the autosomes) and X and Y (the sex chromosomes). Females carry two X chromosomes (refer to Figure 1); males carry an X and a Y chromosome.

About one person in every 500 has a rearrangement of their chromosomes called a translocation. People with a translocation are healthy; however when they try and have a baby there is an increased risk of infertility, miscarriage, and in some cases of a baby being born with a severe disability.

These problems occur because the translocation in the parent predisposes to a more severe chromosomal abnormality in a proportion of their embryos. For most translocation couples, more than half of their embryos are chromosomally abnormal.

PGD can be used to choose embryos that have the capacity to form a healthy baby, so that only these embryos are transferred to the uterus.

Screening for chromosome abnormalities

Even when both partners have normal chromosomes, a significant proportion of all embryos are chromosomally abnormal. This is a normal part of human reproduction, but the proportion of chromosomally abnormal embryos increases with the woman’s age. Usually these embryos do not result in a pregnancy, but sometimes they result in a pregnancy that miscarries, or less commonly the birth of a baby with a chromosome disorder such as Down Syndrome.

PGD can be used to identify the chromosomally normal embryos so that couples can transfer the embryos that have the potential to result in a healthy pregnancy. PGD used in this way is sometimes called preimplantation genetic screening (PGS).

PGS may be recommended for individuals or couples who have experienced multiple miscarriages, where repeated ART cycles have been unsuccessful, or where the woman is older. Screening for chromosome abnormalities allows the selection of a healthy embryo for transfer but it cannot fix the chromosome errors in embryos. For couples who have very small numbers of embryos, PGS may not offer any benefit because there are insufficient embryos from which to select.
What does PGD involve?

Although PGD techniques vary, the PGD process usually involves six main steps:

1. ART techniques are used to create embryos. An embryo is formed when the sperm fertilizes the egg. The ART techniques used for PGD are similar to those that are used for the treatment of infertility, although many couples who use PGD are not infertile. For information about ART treatment and ICSI, please refer to the VARTA brochure, What is Assisted Reproductive Treatment (ART)?

2. Embryos created using ART are grown in the laboratory for either three or five to six days. During this time, each embryo grows to become a small ball of cells.

3. Each embryo is then biopsied or tested; a process that involves the removal of one or more cells from each embryo. Approximately one in every 200 embryos does not survive the biopsy, but the remaining embryos continue to grow and develop normally.

4. Genetic testing is performed on the cells that have been removed. There are several different types of genetic tests that can be performed. The time taken to obtain results varies depending on the type of genetic testing being performed. Some tests will provide results in a matter of hours, while other tests will take two to three weeks to complete. Depending on the type of embryo biopsy being performed (i.e. day 3 or day 5/6) and the timeframe taken to obtain results, the embryos are either left to grow in the laboratory or are frozen pending PGD results. Because all cells in an embryo are usually genetically identical, testing one or a few cells provides information about the genetic makeup of the rest of the embryo.

5. Once the results of genetic testing are available, the embryos are sorted into those that are suitable for transfer to the woman’s uterus and those that are not. Embryos that are not suitable for transfer are typically affected by a serious genetic abnormality. These embryos are usually discarded.

6. Usually, one embryo is transferred to the woman’s uterus. If possible, any remaining unaffected embryos are frozen for future use.

Figure 2: Embryo biopsy

Day 3 embryo biopsy

Performed 3 days after fertilization, when the embryo is typically composed of six to eight cells. A hole is made in the outer shell of the embryo and one or two cells are removed for genetic analysis.

Day 5/6 embryo biopsy (blastocyst biopsy)

Performed five or six days after fertilization. By this time, the embryo should have developed to the blastocyst stage, comprising an inner cell mass (which will go on to form the fetus) and trophectoderm cells (which will go on to form the placenta). Approximately five trophectoderm cells are removed for genetic analysis.
What are the challenges of PGD?

PGD is an effective treatment for many couples who wish to avoid having a child with a serious genetic condition, or to increase their chance of having a successful pregnancy. However, PGD also brings with it additional challenges, and for this reason some couples chose not to use PGD. The main challenges of PGD are as follows:

• PGD requires ART treatment, which couples who are fertile do not otherwise need.

• As with all ART treatment, PGD does not provide a guarantee of pregnancy.

• Some types of PGD tests, particularly those that test for specific inherited conditions, require a special test to be designed before ART treatment can commence. This typically takes between three and six months.

• There is a small risk of error with PGD, due to the many technical challenges of testing single cells. Although the risk of error is usually less than 2%, couples who become pregnant using PGD are offered prenatal diagnosis (chorionic villus sampling or amniocentesis) to confirm the PGD diagnosis.

• The effectiveness of PGD depends on the availability of a number of embryos to test. For couples that produce only a small number of embryos, the likelihood of a successful pregnancy is reduced.

• PGD is a relatively new technique. However, current evidence suggests that the risks to the baby are no greater than for other forms of ART. For more information about health risks of ART, please refer to the VARTA brochure, Possible health effects of IVF.

• PGD is expensive. The costs of PGD vary, but the cost of a PGD cycle is typically between two and three times the cost of a standard IVF cycle. At the moment, there is no public funding for PGD.

More information about genetic testing techniques

Genetic testing technologies are evolving at a rapid rate. The two main techniques currently used for PGD are:

Gene sequencing

This involves reading a stretch of letters of the genetic alphabet (A, T, C and G) to look for the presence of a genetic mutation or ‘spelling mistake’. Although in the future it may be possible to test large parts of an embryo’s genome in this way, currently this testing is limited to short sections of DNA where there is a known risk of a genetic mutation. Gene sequencing is used for PGD when a couple is at increased risk of having a child with a genetic disorder.

Chromosome microarray

This is a new form of chromosome analysis that simultaneously looks at thousands of sites across the genome and counts the number of copies of DNA present. In the normal state, there are two copies of each piece of DNA (one from each parent) and so the presence of a section of the genome where there is either one or three copies indicates an underlying chromosome abnormality. Chromosome microarray has largely replaced a previous technique called FISH, and is used to test for chromosome translocations and to screen for non-inherited chromosomal abnormalities. A special type of microarray, called an SNP array, can also be used in some cases when a couple is at increased risk of having a child with a genetic disorder.

For more information visit the Victorian Assisted Reproductive Treatment Authority at www.varta.org.au or phone 03 8601 5250