

Guidelines on Preimplantation Genetic Diagnosis

Prepared by the National Ethics Committee on Assisted Human Reproduction,
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Introduction

Until recently, the only testing option available to couples at risk of conceiving a child with a genetic disorder was prenatal diagnosis. This involves sampling of fetal cells through the placenta (chorionic villus sampling) or the amniotic fluid (amniocentesis). If a fetus is found to be affected by a particular disorder, couples have to decide whether to proceed with the pregnancy or have an abortion.

Preimplantation genetic diagnosis (PGD) is an alternative to prenatal diagnosis, and is distinguished from it by the stage at which decisions have to be made: at the embryonic rather than the fetal stage.

Description of PGD

PGD is a procedure used to test early human embryos for serious inherited genetic conditions and chromosomal abnormalities. PGD involves several steps:

1. the creation of an embryo via *in vitro* fertilisation (IVF)
2. removal of one or two cells from the embryo
3. genetic testing of these cells for specific genetic conditions or chromosomal abnormalities
4. the subsequent transfer of unaffected embryos to a woman's uterus.

PGD can only be used in conjunction with IVF. The technology can be utilised by fertile couples as well as those experiencing fertility problems.

PGD can test for a range of genetic disorders. Examples of familial single gene disorders for which PGD has been used are:

- Cystic fibrosis
- Thalassaemia
- Spinal muscular atrophy
- Huntington's disease.

Examples of familial sex-linked disorders for which PGD has been used are:

- Fragile-X syndrome
- Haemophilia
- Duchenne's muscular dystrophy.

Examples of familial chromosomal disorders for which PGD has been used are:

- Reciprocal translocations
- Robertsonian translocations.

Examples of conditions that can result from non-familial chromosomal disorders are:

- Down syndrome (an extra chromosome 21)
- Turner's syndrome (females with one X-chromosome instead of two).

PGD and human leukocyte antigen (HLA) tissue typing have been used to identify a suitable tissue match for children affected by familial single gene disorders such as Fanconi's anaemia.¹

PGD Policy Development and Review

In June 2003, the Minister of Health approved the use of PGD in principle and requested NECAHR develop guidelines on the use of this technology.

During 2003/04 NECAHR developed guidelines for providers of fertility services on the use of PGD. The guidelines are based on a thorough consideration of the ethical complexities of PGD. The Committee acknowledges that there are different ethical views regarding the use of PGD in New Zealand. Having considered these different views the Committee believes that the use of PGD as covered by the guidelines is ethically acceptable.

In October 2004, the Committee released the proposed guidelines for public consultation and invited written and oral submissions. NECAHR received submissions from a variety of different groups and individuals with an interest in PGD. Oral hearings were held in Wellington and Christchurch and a Māori focus group was held in Wellington. During the consultation period a diverse range of views was expressed on assisted human reproductive technologies, genetic testing, and the moral status of the embryo, as well as on PGD. These ranged from strong support of the guidelines to total rejection of all reproductive technologies, including PGD. The pluralistic nature of New Zealand society means that universal agreement on the use of PGD was not a possibility. In revising the guidelines following the public consultation, NECAHR took account of all the submissions and focused on the strength of the arguments with regard to particular clauses in the guidelines, rather than on the number of stakeholders for or against them.

In March 2005, the Minister of Health approved the finalised PGD guidelines. The guidelines will be reviewed no later than 2007 and NECAHR welcomes comments from providers and the public on the guidelines since these may assist in their future review.

PGD and Disability

Concern has been raised that PGD discriminates against people with disabilities, and promotes the view that the birth of people with disabilities should be prevented. However, it is important to distinguish between 'disability' and 'people with disabilities', and that selecting against embryos with disabilities does not necessarily imply that those with disabilities are living lives that are either less valuable or less meaningful. NECAHR supports the *New Zealand Disability Strategy* and considers that New Zealand should

¹ For further information on PGD see, National Ethics Committee on Assisted Human Reproduction, *Guidelines for Preimplantation Genetic Diagnosis in New Zealand: Consultation Document*, September 2004.

continue to recognise its obligations to support disabled people and continue to work towards the removal of barriers to full participation in society.

Ongoing Research and Monitoring of PGD

In recent years, concerns have been raised about the relationship between assisted human reproduction techniques and congenital disorders. Although the short-term risks of assisted reproductive procedures are reasonably well-known, the long-term health outcomes of children born as a result of these techniques is still a relative unknown. The Ministry of Health has established an interim advisory group on assisted reproductive technology (ART) to examine the long-term health risks of ART. Long-term follow-up of children born after PGD can provide data on their health and developmental outcomes and contribute to international understanding of the safety and effectiveness of the technique.

The number of children born in New Zealand following the use of PGD is likely to be low. Therefore, NECAHR encourages New Zealand PGD providers to use the European Society for Human Reproduction and Embryology PGD Consortium as an avenue for worldwide collaboration and a way to promote best practice for PGD providers.

Section One – Uses of PGD Not Requiring NECAHR Approval

Familial Single Gene Disorders

1. PGD for familial single gene disorders may be carried out where:
 - 1.1 the disorder has been identified in the family/whānau *and*
 - 1.2 there is a 25% or greater risk of an affected pregnancy *and*
 - 1.3 there is evidence that the future individual may be seriously impaired as a result of the disorder.

Familial Sex-linked Disorders

2. Sex determination for familial sex-linked disorders may be carried out where:
 - 2.1 the disorder has been identified in the family/whānau *and*
 - 2.2 there is a 25% or greater risk of an affected pregnancy *and*
 - 2.3 no specific test for the particular mutation that causes the disorder is available *and*
 - 2.4 there is evidence that the future individual may be seriously impaired as a result of the disorder.

Familial Chromosomal Disorders

3. PGD for familial chromosomal disorders may be carried out where:
 - 3.1 the disorder has been identified in the family/whānau *and*
 - 3.2 there is evidence that the future individual may be seriously impaired as a result of the disorder.

Non-familial Chromosomal Disorders Associated with Advanced Reproductive Age

4. PGD for non-familial chromosomal disorders (aneuploidy testing) may be carried out where:
 - 4.1 the woman is of an advanced reproductive age.

Non-familial Chromosomal Disorders Associated with Infertility

5. PGD for non-familial chromosomal disorders (aneuploidy testing) may be carried out where:
 - 5.1 the woman has had recurrent implantation failure or recurrent miscarriage.

Determination of a Serious Disorder

6. It is the responsibility of PGD providers, in collaboration with a clinical geneticist, to determine whether a disorder is likely to be serious in the offspring.

Section Two – Uses of PGD Requiring NECAHR Approval

PGD with Human Leukocyte Antigen (HLA) Tissue Typing

7. HLA tissue typing in conjunction with PGD must be submitted to NECAHR for ethics approval on a case-by-case basis and may only be carried out where:

Affected Child

- 7.1 the affected child suffers from a familial single gene disorder or a familial sex-linked disorder *and*
- 7.2 no other possibilities for treatment or sources of tissue are available *and*
- 7.3 the planned treatment for the affected child will utilise only the cord blood of the future sibling *and*

Embryo

- 7.4 the embryo will be a sibling of the affected child *and*
- 7.5 the embryo is at risk of being affected by a familial single gene disorder or a familial sex-linked disorder for which a PGD test is available *and*

Family/Whānau

- 7.6 the health and wellbeing of the family/whānau has been fully considered.

Section Three - Prohibited Uses of PGD

8. PGD may not be carried out for the following:
 - 8.1 social reasons, including sex selection
 - 8.2 to alter the genetic constitution of an embryo
 - 8.3 to select embryos with a genetic impairment seen in a parent
 - 8.4 any reason other than those specified in sections one and two.

Section Four – Information and Counselling

Information

9. Providers must ensure that those seeking PGD are given all of the information relevant for informed decision-making, and this must include reference to the following:
 - 9.1 the processes and procedures associated with IVF and PGD
 - 9.2 the risks associated with the procedures
 - 9.3 the background and experience of the clinic and clinicians
 - 9.4 the success rate of the procedure, both in general, and at that particular clinic
 - 9.5 the alternatives to PGD.
10. Providers must ensure that those seeking PGD are given all of the following information prior to giving consent:
 - 10.1 genetic and clinical information about the specific disorder/infertility
 - 10.2 the likely impact of the disorder/infertility on those affected and their families/whānau
 - 10.3 information about treatment, counselling, and the extent of community and social support available
 - 10.4 the availability of prenatal testing following successful implantation
 - 10.5 NECAHR's requirement for providers to supply information for the Committee's annual report as specified in guideline 17.

Counselling for People with Familial Disorders

11. Providers must ensure that those seeking PGD for familial disorders receive genetic and psychosocial counselling from qualified counsellors who are trained in genetic counselling.
12. Counselling must be culturally appropriate and include consideration of the following:
 - 12.1 the nature of the disorder, its likely impact on the offspring and family/whānau and the availability of treatment
 - 12.2 the family/whānau experience of the genetic disorder
 - 12.3 the range of alternatives to PGD and subsequent decision-making processes
 - 12.4 the possible implications of undertaking PGD.

Counselling for People with Non-familial Disorders

13. Providers must ensure that those seeking PGD for non-familial disorders receive psychosocial counselling from a qualified counsellor.
14. Counselling must be culturally appropriate and include consideration of the following issues:
 - 14.1 the range of alternatives to PGD and subsequent decision-making processes
 - 14.2 the possible implications of undertaking PGD.

Section Five – Procedural Requirements

Accreditation

15. All clinics wishing to provide PGD must be accredited by, and meet any requirements regarding the provision of PGD of, the Reproductive Technology Accreditation Committee of the Fertility Society of Australia.

NECAHR Approval

16. All clinics wishing to provide PGD must apply to NECAHR for approval using the innovative treatment application form.

Annual Reporting

17. Each clinic that is given approval to perform PGD must submit an annual report to NECAHR, which will include:
 - 17.1 the number of PGD procedures carried out for familial disorders, and the genetic condition for each procedure
 - 17.2 the number of PGD procedures carried out for non-familial disorders, and the medical indications leading to the use of PGD
 - 17.3 the outcomes of each procedure (to be reported in the following year), including results from any subsequent genetic testing
 - 17.4 any ethical issues that have arisen during the course of treatment
 - 17.5 any issues that have emerged during counselling that could have long-term impact on the offspring and their family/whānau.