Chapter 3
Genetic Counselling and Its Role in PGD

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PGD has now been available for over two decades and the number of patients treated has increased annually. The process is by nature complex and requires a high level of clinical and laboratory understanding, including the practicalities of assisted reproduction treatment, some aspects of which may be unfamiliar to even experienced geneticists and genetic counsellors. The PGD Consortium of the European Society of Human Reproduction and Embryology (ESHRE) and the Preimplantation Genetic Diagnosis International Society (PGDIS) recommend that acceptable practice requires that the counselling should be offered to all couples requesting PGD and is provided in a nondirective manner by an appropriately qualified professional. The combined skills of genetic counsellors and clinical geneticists from accredited genetic centres, working together with specialists in assisted reproductive medicine, should ensure that patients receive a high-quality service in PGD.

Most couples will have experienced the loss of a child or a pregnancy and possibly had prenatal diagnosis (PND). They are generally united in their wish to have a child that is

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biologically related, but is unaffected by the genetic disorder within the family. The most commonly cited reason for using PGD is to avoid termination of pregnancy. For others, the advantage of PGD is the knowledge that from very early on in gestation, the pregnancy is unaffected. Therefore, it is an essential part of the PGD genetic counselling process to establish the reason for choosing PGD to ensure that couples' expectations can reasonably be met.

The aim of genetic counselling is to deliver accurate information alongside the support given to patients to enable them to make the most appropriate decision for them personally, whilst ensuring as far as possible that no pressure is applied from clinical professionals involved in their care. Genetic counselling services vary in structure being delivered by a combination of medically qualified clinical geneticists and genetic counsellors with a nursing or science background and a Master's level degree in a related field.

Genetic Counselling Before a Treatment Cycle

Before a couple is referred for PGD, they will have usually consulted a clinical geneticist to discuss the implications of the genetic condition affecting their family. Such consultations provide patients with information about the condition, recurrence risks, contemporary appropriate genetic testing, discussion of reproductive options, organisation of family follow-up and support in coming to terms with the diagnosis.

Prior to the start of a PGD treatment cycle, it is important that couples:

- Discuss their family history and reason for requesting PGD
- Understand their genetic risk
- Know what alternative reproductive options are available
- Understand the PGD process and the side effects of treatment

- Understand the limitations of testing and success rates
- Consider the physical, psychological and financial impact of treatment
- Receive a written summary of the consultation and relevant patient information leaflets

Genetic Counselling Is Not the Same as Infertility Counselling

Although IVF is used in both procedures, and some couples may have experienced childlessness due to repeated miscarriage, or incidentally as result of their genetic condition, e.g. Klinefelter syndrome or Turner syndrome, the expertise of the genetic counsellor is in helping couples to better understand their genetic condition and prepare for PGD as a means of avoiding transmission.

Counselling Issues Specific to PGD

Welfare of the Child

In accordance with the UK Human Fertilisation and Embryology Act (2008), centres treating couples are responsible for ensuring any assisted reproductive treatment offered and must take account of the welfare of any children born as a result. Some couples requesting PGD will be affected with the genetic disorder in their family and have associated clinical symptoms. A condition such as cystic fibrosis may be life limiting or, in the case of Huntington disease (HD), associated with long-term progressive disability. Such issues require discussion with the couple to establish how they would manage in the event that one parent is no longer able to care for a child and the unaffected partner becomes the carer or the affected parent dies whilst the child is at a young age.

Impact of Treatment on the Family

A family caring for a child with a disability needs to consider the impact of travel to appointments and the rigorous demands of the treatment schedule. The risk of ovarian hyperstimulation syndrome with the possibility of hospitalisation must also be considered. Couples should always be encouraged to establish support networks to ensure backup if there are complications associated with treatment.

Choices at Embryo Transfer

Number of Embryos to Be Transferred

The number of embryos used in transfer continues to court controversy in the world of assisted reproduction because of the perceived improvement in chances of cycle success with the transfer of two embryos versus the increased chance of multiple birth. Twins and triplets add another dimension of difficulty to couples seeking PGD; as well as the physical hazard to both mother and babies associated with twin or triplet birth; the social and psychological impact of a multiple birth is considerable. Many of the couples that request PGD already may be caring for children with disabilities. The introduction of more than one further child therefore needs careful consideration in relation to the potential impact on the family. Prolonged hospital stay and the risk of damage or disability from prematurity may further add to the burden.

Carrier Status

Since embryos that carry one copy of a recessive gene or females in X-linked disorders generally are unaffected by the disorder being tested, they can be recommended for transfer. Excluding carrier embryos reduces the cohort of transferable embryos which in turn could compromise the success rate of treatment. Couples are usually fully informed of the disease status of all their embryos and should also have been made aware whether there is any significant risk to transfer of

carriers – see below. However, this information may conflict with recommendations for carrier testing in childhood, an issue that has been debated within the genetics community for many years. The report "Genetic Testing in Childhood" recommends that unless there are clinical benefits to testing minors, testing for carrier status should be delayed until a child is old enough to understand the implications and be part of the decision making. In addition, since prenatal diagnosis generally is offered as a means of confirming the PGD result, or should that be declined, by umbilical cord blood testing at birth, it is important that the issue of childhood testing is discussed with couples before carrier status is attributed to an embryo, fetus or neonate.

Sex Selection

Sex selection on social grounds is prohibited in most European countries and in the UK under the terms of the HFE Act (2008), but is freely allowed in some countries (Jordan) or condoned in others (USA). However, when undertaking PGD for X-linked disorders, the laboratory will be able to determine the sex of the embryos as well as their disease status. In some conditions where carrier females may have a clinical phenotype (e.g. as in the case of Fragile X or haemophilia A/B), there may be good clinical grounds for not transferring carrier embryos. Embryos that are genetically suitable for transfer should always be prioritised on the basis of their morphological quality and potential for implantation. However, in the absence of a clinical phenotype associated with carrier status, couples could be aware of the sex of their embryos and should be given the option *NOT* to know the sex of their embryos.

Genetic Counselling After a PGD Cycle

Successful Cycle and Confirmation of Diagnosis

Following a successful PGD cycle and confirmatory first trimester viability scans (Chap. 9), the couple should be contacted by the genetic counsellor to discuss the option of

confirmatory prenatal diagnosis. All PGD cases have a small risk of misdiagnosis, which will vary depending upon the test used, the skill of the centre offering treatment and the condition for which PGD was offered. Chorionic villus sampling (CVS), amniocentesis and anomaly scanning are all possible and widely available options. For many couples confirmatory testing is difficult issue to confront, as they are reluctant to put the pregnancy at risk from invasive testing. As many couples have used PGD to avoid the issue of termination, the prospect of having to face this possibility after prenatal diagnosis leads many to decline confirmatory testing. Collecting an umbilical cord blood sample at birth provides an alternative means to confirm successful avoidance of the genetic condition, although many centres will not offer this option in PGD for Huntington disease. As these couples often decline prenatal diagnosis, confirmatory testing at birth could result in mutation detection in a child, should a misdiagnosis have occurred and would contravene current clinical guidelines which advocate against testing of minors for late onset conditions since the child has not had an opportunity to consent to such testing.

Unsuccessful Cycle and Follow-Up

Around 30 % of PGD cycles will not result in embryo transfer due to:

- Poor response to ovarian stimulation
- Failure of fertilisation
- Poor embryo quality incompatible with biopsy
- Absence of genetically suitable embryos for transfer

Other couples will have a negative pregnancy test after embryo transfer or suffer an early pregnancy loss following a positive test. Each of these is a disappointing and often distressing outcome for couples. These couples should always be offered a follow-up appointment as soon as possible to discuss the outcome of the cycle, and where appropriate to discuss any future treatment planned. Some may have embryos cryopreserved for additional attempts at transfer, whilst for others the advice may be that further cycles are not recommended

where the chance of success is considered too low. Such discussions need sensitive counselling and involvement of the rest of the PGD team. Genetic counsellors can support the couples at or after these consultations and liaise with the couple's local genetic centre where necessary.

Paediatric Follow-Up

In most cases, a successful PGD cycle will result in an ongoing pregnancy and a healthy live born infant. Although PGD is a well-established clinical service, outcome data on babies born is limited (see Chap. 11 and 18). Long-term follow-up and data collection have been recommended since the early days of PGD. The ESHRE PGD consortium recommends paediatric review at birth, 1 and 2 years of age. This can be organised via the PGD centre involved in the treatment of a couple or on a more local basis following referral to a paediatrician.

Recent ESHRE PGD consortium data reported that no malformations were detected in 95 % of PGD babies. Abnormalities were varied and ranged from significant cardiac abnormalities to mild syndactyly. Longer-term studies seem to reflect that growth and developmental parameters in PGD children are equivalent to IVF/ICSI children and normal controls.

Key Points

- Genetic counselling is an integral part of the PGD process.
- Genetic counselling is not the same as fertility counselling.
- Couples should have access to genetics expertise from the point of referral to monitoring of babies born following treatment.
- In accordance with recommended practice guidelines, appropriately qualified personnel should be employed to work as members of the PGD team.

Further Reading

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