

Preimplantation Genetic Diagnosis Huntington disease exclusion testing Supplementary leaflet

This leaflet has been created as an additional source of information, to be read in conjunction with the **Preimplantation Genetic Diagnosis Booklet**. The details within the following pages are specific to you and the reason why you have asked about PGD treatment.

As before, there will be plenty of time to discuss further aspects of treatment during your consultation, but if anything is unclear in the leaflet, please let us know. Our contact details can be found on page 33 of the main booklet.

The **Preimplantation Genetic Diagnosis Booklet** explains what happens up to the stage where a cell is removed from each embryo. This leaflet explains the testing that is done to determine which embryos are at risk or not at risk of Huntington disease (HD).

Exclusion PGD. This is a preimplantation test for those couples when one partner is at 50% risk of HD, but does not wish to be tested. We look at markers on chromosome 4 (a type of DNA fingerprinting) near the HD gene and can distinguish low risk from high risk embryos.

Although we have experience of offering PGD for other genetic conditions, there are some special issues, associated with HD which are different from those of other disorders that require careful thought. **Before** deciding whether you wish to come and meet us to discuss PGD for HD we would ask you read this leaflet. We appreciate that following this you may have a number of questions. If so please do contact one of the team members listed overleaf who will be able to help.

Testing for high and low risk embryos in PGD

There are two steps to obtaining the genetic material (DNA) needed for the test.

1. The DNA is extracted from each single embryo cell and copied a million times (this is called whole genome amplification). This gives us a large sample of DNA to work on.
2. Then the crucial piece of DNA near the HD gene is rapidly copied many times again. This process is called PCR (polymerase chain reaction).

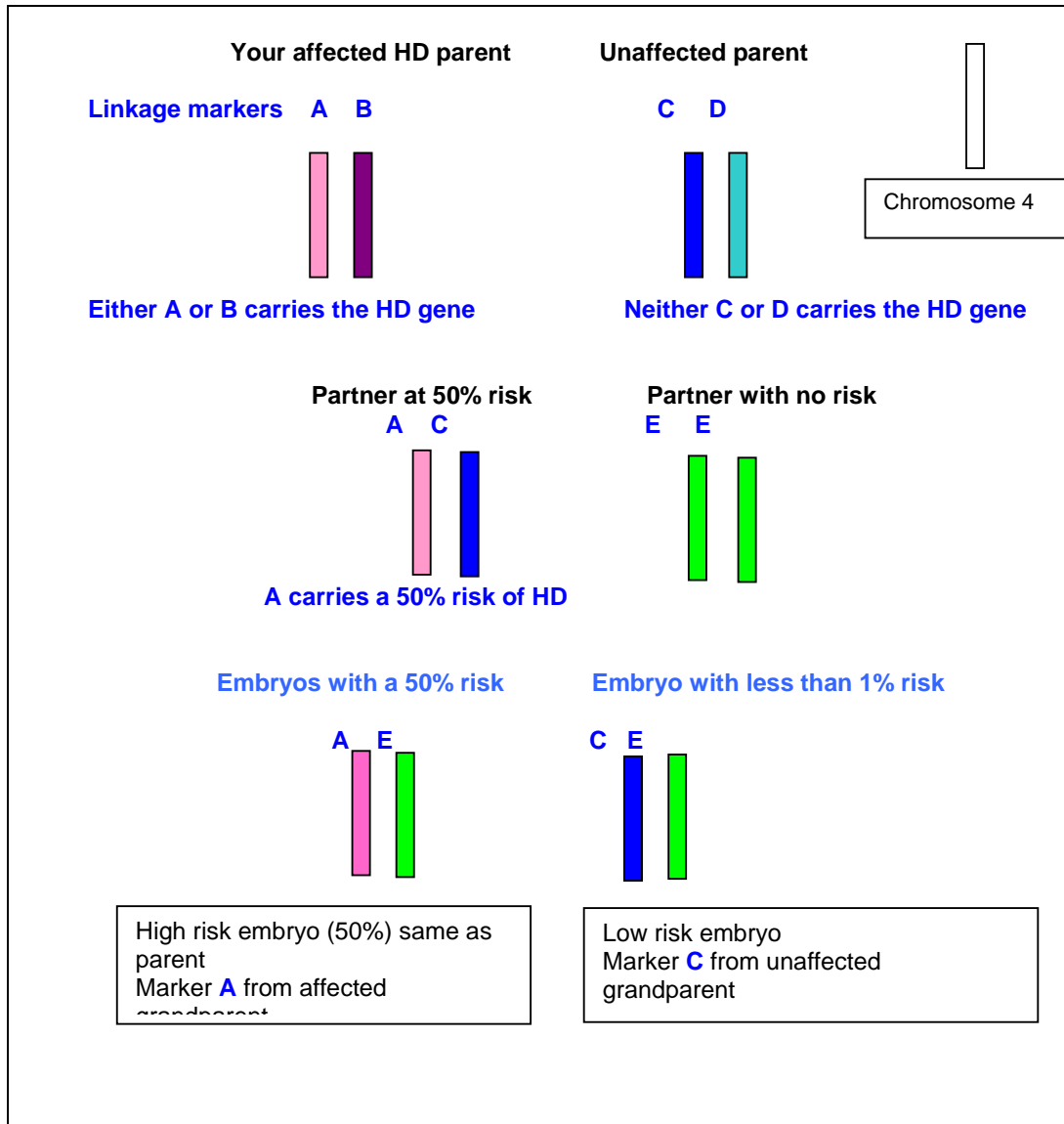
Now we have enough DNA to do the testing.

In order that we can undertake PGD for you, and to ensure that the results are as accurate as possible, we must look at the DNA in samples from **both** of you. We also need DNA from one or other (preferably both) of the **parents of the partner who is at 50% risk of HD**.

When offering HD exclusion PGD, we shall **not** be looking for the size of the HD gene in the embryos that are created because that would provide us information about whether or not you carry the gene for HD. Instead, we use a technique called linkage analysis.

This is similar to DNA fingerprinting which simply enables us to tell the difference between markers on the two chromosome 4s which you carry. To do the test we need to trace these markers through two generations, which is why we will need blood samples from one or ideally both of the at-risk person's parents. This does mean that you may have to ask your parents for blood samples. Sometimes we are lucky and can obtain DNA that has been stored from blood samples that your parents had taken previously. This diagram helps to explain how we do the tracing.

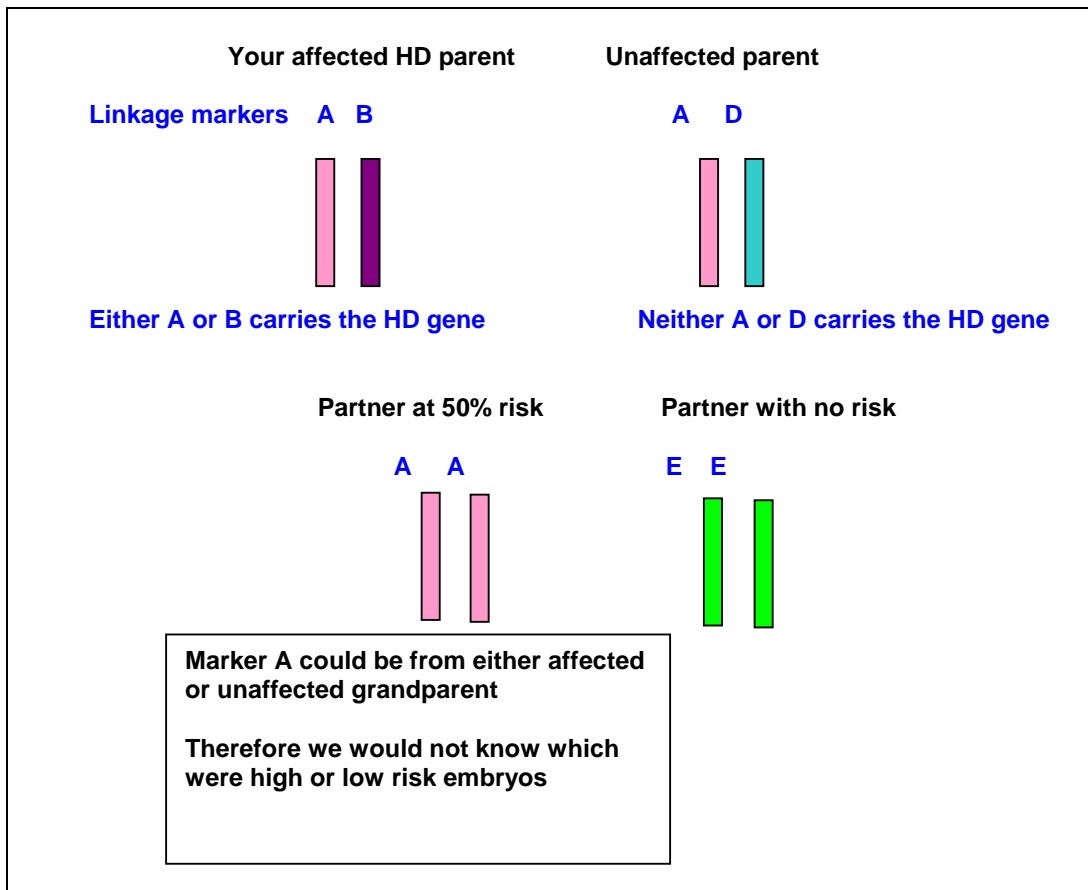
Diagram 1- showing how linkage analysis works



When we test the samples we obtain one of 2 results

- **Informative-** where we can tell the markers on the chromosome 4s apart. We can only offer you PGD if we can do this (Diagram 1).
- **Uninformative-** Sometimes we are unable to tell the markers apart (Diagram 2). If this is the case we will not be able to tell whether an embryo is at risk of HD or not. In this situation we cannot offer PGD.

Diagram 2- showing how results can be uninformative



Fortunately in most cases the sample work up is informative and we can offer couples PGD.

Outcome of embryo testing

If the testing prior to treatment is informative then in any cycle of PGD there may be a combination of the following results in the embryos tested:

- Embryo inherits the high risk marker and has a 50% risk of HD (Diagram 1)
- Embryo inherits the low risk marker and has less than 1% risk of HD (Diagram 1).
- The test has failed to give a clear result in the embryo.

The only embryos that will be considered as suitable for use will be those that are **clearly low risk**.

Accuracy of the test

Whilst the greatest care is taken to ensure that the diagnosis is as accurate as possible, nevertheless there is a chance that the result could be incorrect in the embryo analysed. Fortunately, the chances of this happening are small, but the actual risk will be discussed with you in detail at a later stage once we have the results of your blood tests. As a guide, the risk will be around 1% (1 in 100) per embryo.

Confirmation of diagnosis

Should a PGD cycle be successful and you become pregnant following transfer of your unaffected embryos then we would offer you a test in your pregnancy to ensure that the diagnosis is correct. This test could either be a chorionic villus sample at 11 weeks of pregnancy or an amniocentesis at 16 weeks of pregnancy. We appreciate that after going through such a procedure as PGD this can be a difficult decision to make, but if you decline confirmatory prenatal testing then **no** further testing will be offered following delivery of your baby. If we tested a baby after birth we could be performing a predictive test on a child without their permission and this would be against the UK Guidelines on Predictive Testing.

Limitations of testing

Testing the embryos is limited to offering a test for HD. It is not possible to undertake any other testing on the single cells simultaneously, e.g. Down syndrome. The chances of any other problems affecting your embryos would be the same as for any other couple in the general population. The incidence of Down syndrome does increase with a woman's age and this may be something for which you may want to have a prenatal test, if you were to become pregnant.

Welfare of the child

Our Centre is licensed to practise PGD by the Human Fertilisation and Embryology Authority (HFEA). They regulate PGD in accordance with the Human Fertilisation and Embryology Act. As part of the Act we are required to consider the welfare of any potential child when offering general fertility treatment or PGD to a couple. This means that you need to consider what the effects could be on you and your child, if over time you do develop symptoms of HD.

We appreciate that even if you do carry the gene for HD you may still be free of HD symptoms for many years. However if symptoms do start then you may need to think about how this might affect the care of your child. You may wish to make provision for this. In order to enable us to help you with your planning we will offer you an appointment with a neurologist for an examination prior to PGD treatment. Some couples may find this helpful in their planning for having a family, although we appreciate it can be a major step when you have taken the decision not to be tested for HD in the first place. You may, therefore, decline this offer.

We have fertility counsellors who are available should you wish to speak to them about any issues arising from PGD. This is available for you as a couple or for each of you individually.

Other useful contacts

Huntington Disease Association

Down Stream Building,
1, London Bridge,
London,
SE1 9BG
Tel: 020 7022 1950
Email: info@hda.org.uk
www.hda.org.uk

Glossary

Amniocentesis: Test done during pregnancy. A fine needle removes fluid from the amniotic sac at about 16 weeks of pregnancy. This test is usually performed to check for abnormalities in the fetus.

Chorionic villus sampling (CVS): Test done during pregnancy. Fine needle removes some tissue from the placenta (afterbirth) at about 11 weeks of pregnancy. This test is usually performed to check for abnormalities in the fetus.

Factual information presented within this communication is based on accurate contemporaneous peer reviewed literature. Evidence of sources can be provided on request.