

Preimplantation Genetic Diagnosis Huntington disease 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 have or do not have the Huntington disease (HD) gene.

Although we have experience of offering PGD for other genetic conditions, there are some special issues, associated with HD which are different to those in other disorders that require careful thought. **Before** deciding whether you wish to come and meet us to discuss PGD for HD we would ask that 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 HD 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 which contains 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.

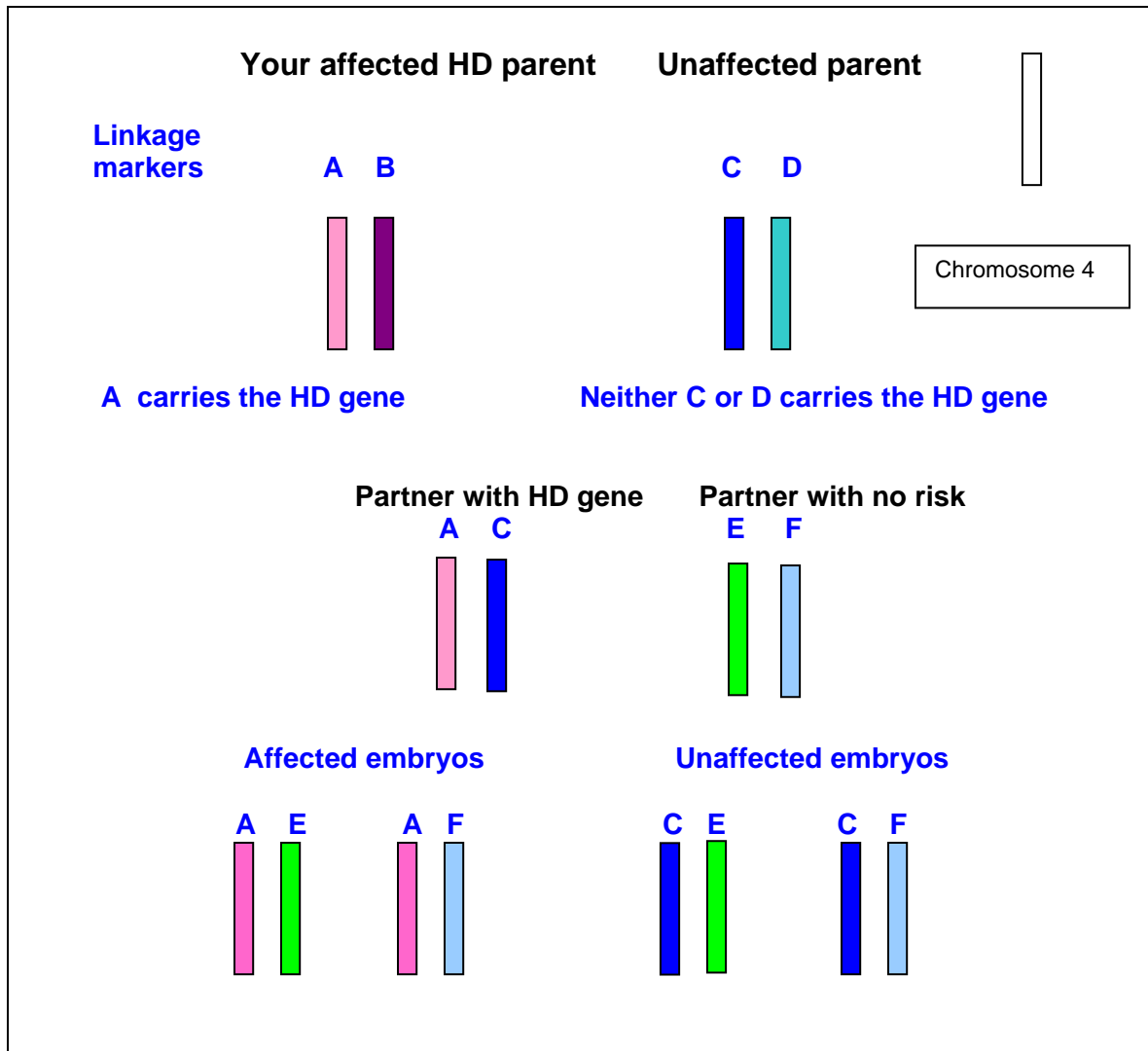
In order that we can undertake PGD for you, and to ensure that the results are as accurate as possible, we must look at the DNA in samples from **both** of you. We also need DNA from one or other (preferably both) of the **parents of the partner who has the HD gene**.

When offering HD PGD, we shall **not** be looking for the size of the HD gene in the embryos, instead we use a technique called linkage analysis.

This is similar to DNA fingerprinting which simply enables us to tell the difference between the two chromosome 4s which you carry. To do the test we need to trace “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 tracking.

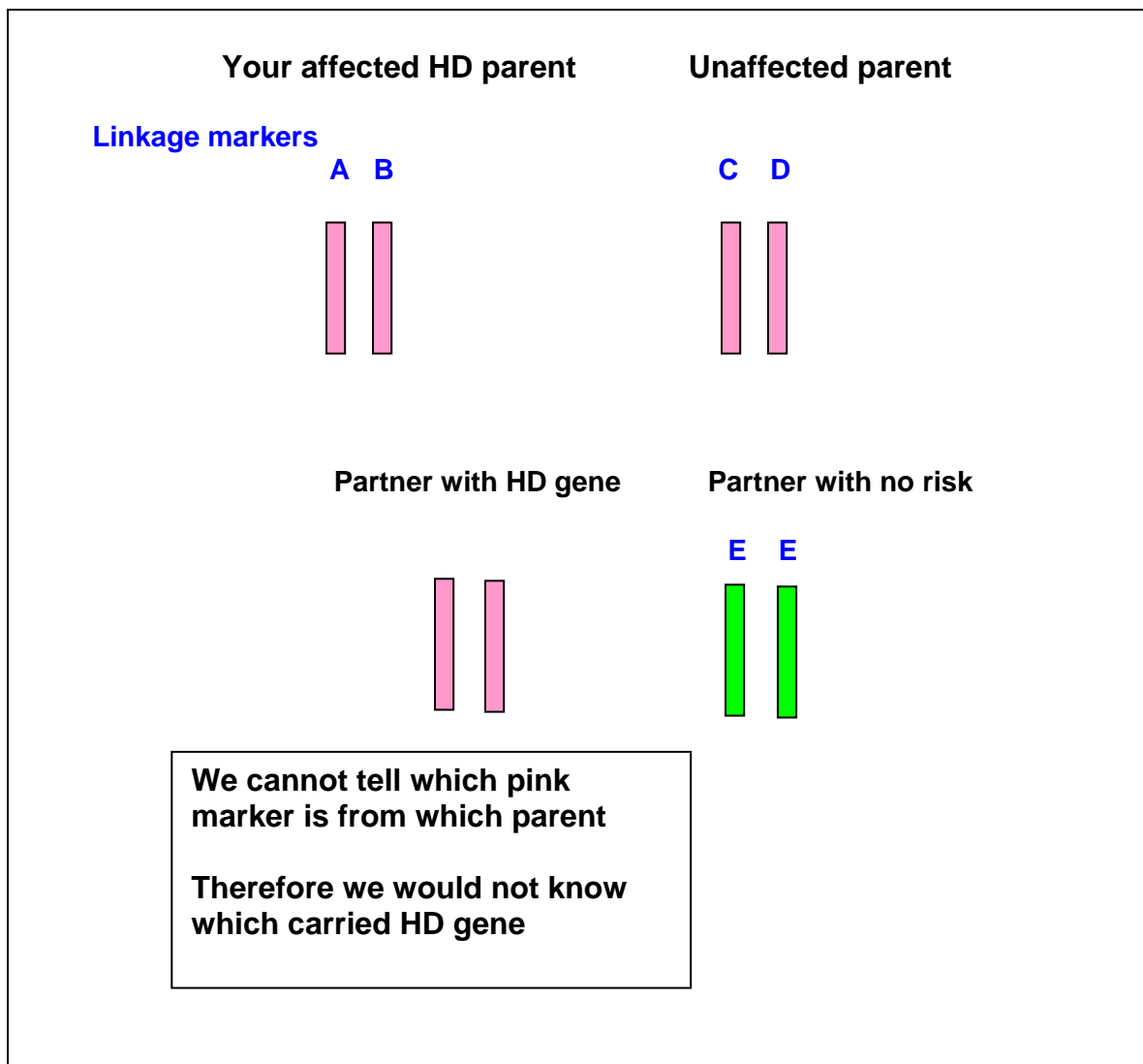
Diagram 1- showing how linkage analysis works



When we test your samples before starting PGD 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, as in the diagram above.
- **Uninformative-** Sometimes we are unable to tell the markers apart (see diagram below). 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 sometimes results are uninformative



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

Outcome of embryo testing

In any one cycle of PGD there may be a combination of the following results:

- Embryo has inherited the HD gene markers and is affected (diagram 1)
- Embryo has inherited the normal markers and is unaffected (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 unaffected**.

Accuracy of the test

Whilst the greatest care is taken to ensure that the diagnosis is as accurate as possible, there is a chance that the result in the embryo analysed, could be

incorrect. Fortunately, the chances of this happening are relatively small, but the actual risk will be discussed in detail with you at a later stage when we have the results of your blood tests. As a guide, the risk will be between less than 1% (1 in 100) per embryo.

Confirmation of diagnosis

As PGD is not 100% reliable, we offer couples that become pregnant following treatment a prenatal test (test in pregnancy) to confirm the diagnosis. This may be a CVS (chorionic villus sampling) done at 11 weeks of pregnancy or an amniocentesis done at 16 weeks.

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. Usually people who decline prenatal testing do so because they would not terminate an affected pregnancy or they are concerned about the risk of miscarriage associated with the test. If we tested a baby after birth, we would be performing a predictive test on a child 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 by the Human Fertilisation and Embryology Authority (HFEA). They ensure that we carry out PGD in accordance with the Human Fertilisation and Embryology Act and the HFEA Code of Practice. As part of the Act we are required to consider the welfare of any child who may be born when offering general fertility treatment or PGD to a couple. This means that you need to consider what the effects will be on you and your child when the carrier of the gene develops symptoms of HD.

We appreciate that despite having a gene positive test you may be free of HD symptoms for many years, but if symptoms do start then you may need to think about how this may affect the care of your child. You may wish to make provision for this. If you felt that it would help you with your planning to know whether or not you already have symptoms then we can arrange an appointment for you to see a neurologist for an examination prior to PGD treatment.

Although it is difficult to make predictions about how quickly symptoms will develop, some people find it helpful for plans to be put in place for a child in the future. To help with this further, we will also discuss this issue with you in more detail, usually during your second PGD appointment. We have fertility

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

There will plenty of time to discuss the issues above and those in the **Preimplantation Genetic Diagnosis Booklet** when you attend the clinic, but in the meantime, if you have other questions please ring us on the contact numbers given in the main leaflet.

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.

