

Preimplantation Genetic Diagnosis Von Hippel Lindau Syndrome 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 Von Hippel Lindau (VHL) gene.

Although we have experience of offering PGD for other genetic conditions, there are some special issues, associated with VHL 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 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 embryos for VHL

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 VHL gene is rapidly copied many times again. This process is called PCR (polymerase chain reaction).

Now we have enough DNA to do the testing.

You may remember that VHL is caused by changes in the VHL gene (this gene is found on chromosome number 3). There are different types of changes in the gene that cause VHL (e.g. deletion, missense mutation, point mutation). All our chromosomes and genes come in pairs and we all have two copies of the VHL gene. In an affected person there will be one normal copy and one changed copy of the gene.

Linkage analysis

Linkage analysis compares genetic markers in your DNA with genetic markers in the embryos' DNA. We can then tell the chromosomes apart and see the difference between the one carrying the changed VHL gene and the one carrying the normal VHL gene.

Linkage analysis tells us two pieces of information:

1. The test tells us whether the embryos are affected or unaffected with VHL.
2. That the cell being tested is definitely a cell from your embryo and not from another source.

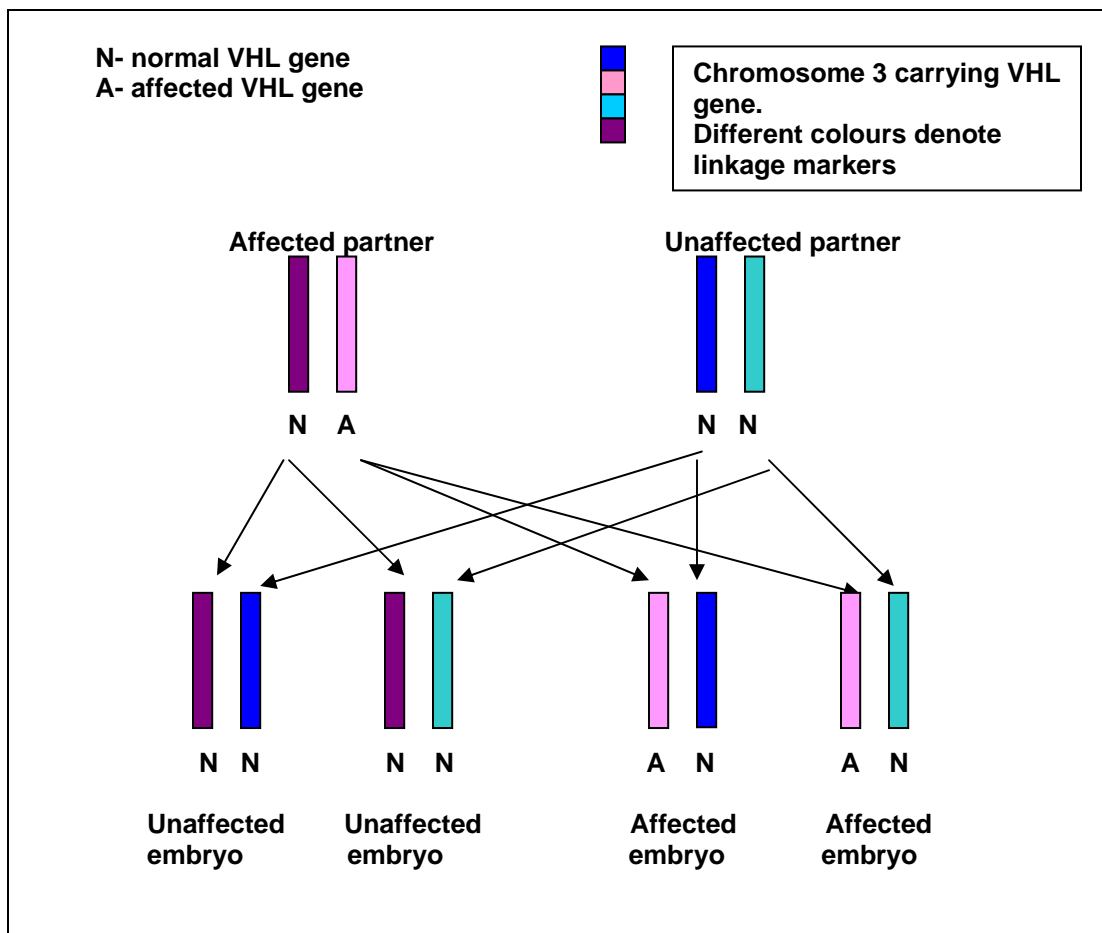
To be able to offer linkage analysis we will require blood samples from the two of you and other family members who may be either affected or unaffected by VHL.

Outcome of testing

Results in your embryos

It is likely that the results we obtain will be a combination of the following (see diagram below):

Diagram to show possible outcomes of PGD



Outcome of embryo testing

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

- An embryo has two copies of the normal chromosome 3 and is **unaffected**.
- An embryo has one copy of the normal chromosome 3 and one copy of the affected chromosome 3 and is **affected**.
- The test result in an embryo is inconclusive.

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. If you decide against confirmatory prenatal testing then it is possible to check the results following delivery of your baby.

Limitations of testing

Testing the embryos is limited to offering a test for VHL. It is not possible to undertake any other testing on the single cells at the same time, 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 if the carrier of VHL develops significant symptoms and becomes unwell.

We appreciate that despite having a gene positive test you may not have been significantly affected by VHL at present. If symptoms develop and require treatment then you need to think about how this may affect the care of your child. You may wish to make provision for this by planning ahead of time so that support is available for your family should this situation arise.

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.

Health of the affected partner

As women undertaking PGD may become pregnant, it is important that we make sure that if it is the female partner who is affected that she is in good health and there are no associated dangers linked to becoming pregnant. It is likely that at some point prior to treatment we will write to the physicians (doctor) looking after you to make sure that the treatment will not make your health deteriorate in any way.

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

Von Hippel Lindau Support Group

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.

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