

Preimplantation Genetic Diagnosis PGH- Embryo sexing for X linked conditions 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 affected or unaffected by the X linked condition in your family.

Testing your embryos

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 affected gene on the X chromosome 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 the genetic condition in your family is caused by alterations in a gene on the X chromosome. There are many different types of these gene alterations and you may know which one you carry. We all have two copies of the sex chromosomes:

X and **Y** if we are male

X and **X** if we are female.

If there is an altered gene on a boy's X chromosome this will result in him being affected. If a girl carries an altered gene on one of her X chromosomes, the second X chromosome will act as a back up copy. Carrier girls are usually unaffected.

Linkage analysis

The test we now do is also called **preimplantation genetic haplotyping (PGH)**. You may hear this term being used by the PGD team.

Because there are often many different gene alterations causing X linked conditions, it is not possible to look directly for these in the embryo cells. We therefore have to test the embryos in a different way.

PGH helps us get around this problem. It is similar to DNA fingerprinting and compares genetic markers in your DNA on your X chromosomes with genetic markers in the embryos' DNA. We can then tell the X chromosomes apart and see the difference between those carrying the affected gene and those carrying the normal gene. To do this part of the test, we will need to look at blood samples from you and other affected members or carriers in your family.

Linkage analysis tells us two pieces of information:

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

Outcome of embryo testing

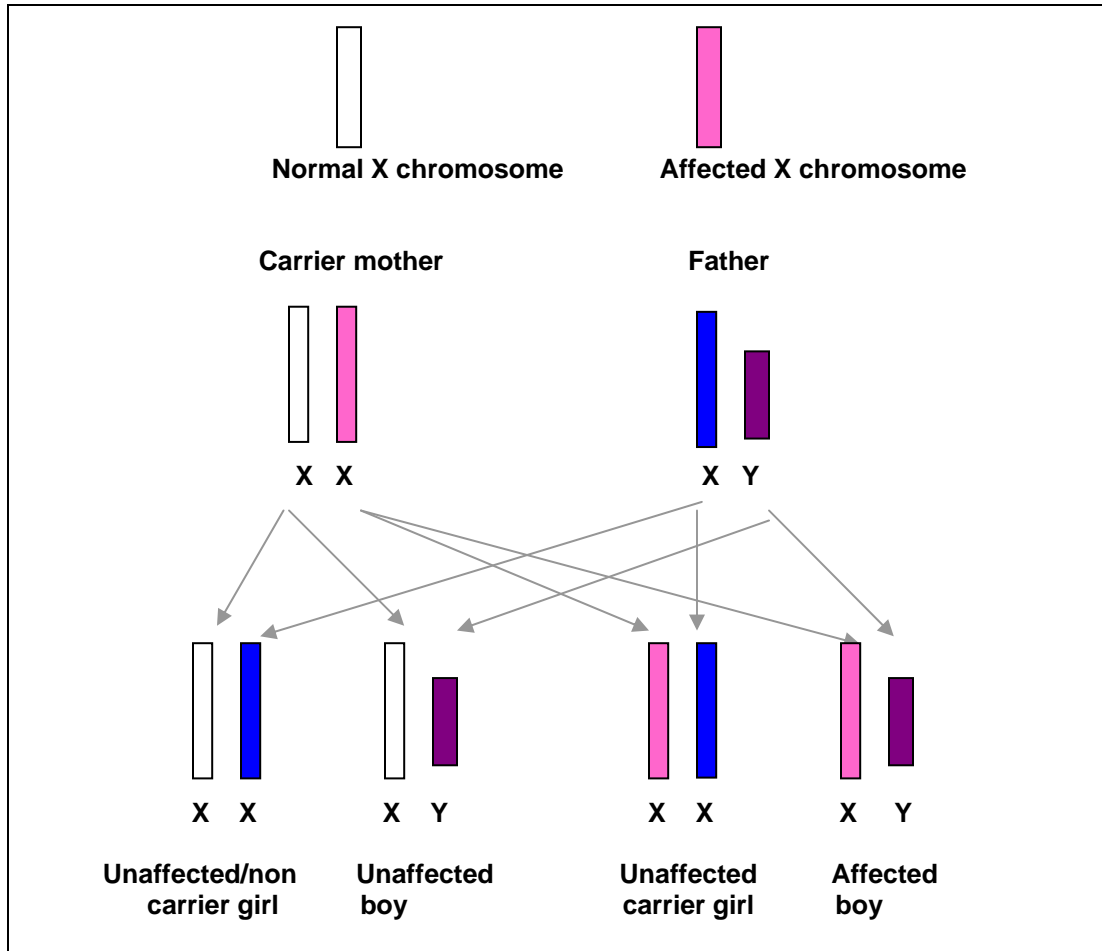
Results in your embryos

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

- An embryo has two copies of the normal X chromosome markers and is an **unaffected female**.
- An embryo has one copy of the normal X chromosome marker and one copy of the affected X chromosome marker and is a **carrier female**.
- An embryo has only one copy of the normal X chromosome marker and is an **unaffected male**.
- An embryo has only one copy of the affected X chromosome marker and is an **affected male**.
- The test has failed to produce a result in the embryo.

The only embryos that will be considered as suitable for use will be those that are **clearly unaffected**. In some cases female carriers will be used, but this will be discussed further when we meet you.

Diagram to show possible outcomes of PGD



The choices with regard to embryo transfer will be discussed further with you at the consultation.

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 chance of this happening is relatively small. This is likely to be less than 1% (1 chance in 100) per embryo.

The actual risk will be discussed with you before you undertake treatment.

Confirmation of diagnosis

As PGD is not 100% accurate, 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 a procedure such as PGD this can be a difficult decision to make. If you decide against confirmatory prenatal testing then we could arrange for a blood sample to be taken from the baby's umbilical cord

at birth. The blood sample will be sent to our laboratory and confirmation of the PGD should be available within a week. Arrangements will be made to contact you with this result.

Limitations of testing

Testing the embryos is limited to offering a test for the specific genetic condition in your family. 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.

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.

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.