

Preimplantation Genetic Diagnosis Hallopeau-Siemens recessive dystrophic epidermolysis bullosa Supplementary leaflet

This leaflet is designed to be read alongside the **Preimplantation Genetic Diagnosis (PGD)** booklet.

The information in this leaflet is specific to Hallopeau-Siemens recessive dystrophic epidermolysis bullosa (HS-RDEB), the reason you have asked about PGD treatment.

There will be plenty of time to discuss the treatment during your consultation, but if anything is unclear in this 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 discover which embryos have the faulty genes that cause Hallopeau-Siemens recessive dystrophic epidermolysis bullosa (HS-RDEB).

Testing for HS-RDEB

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

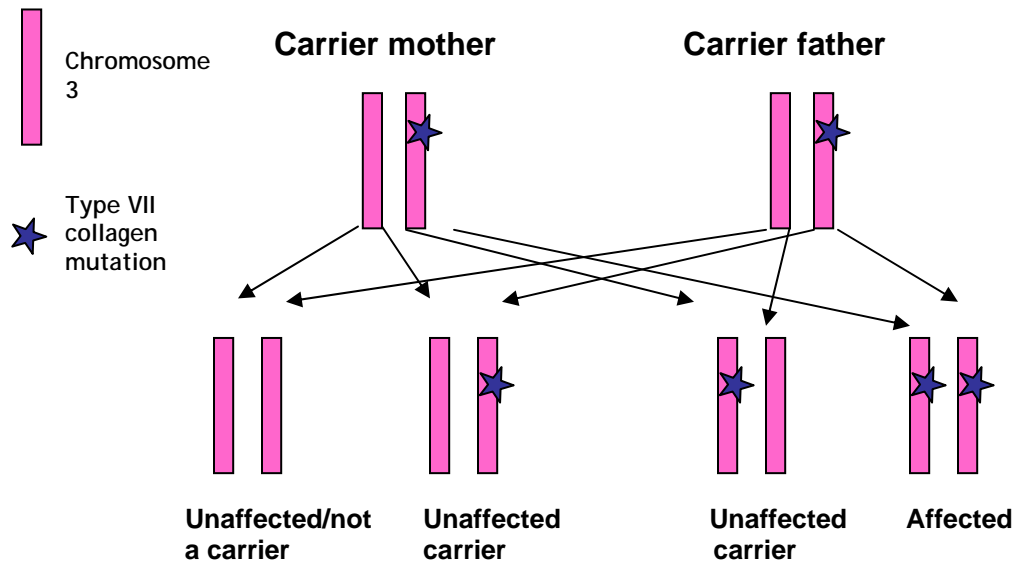
1. The DNA is extracted from each single embryo cell and copied a million times (this is called whole genome amplification). This gives us a large sample of DNA to work on.
2. Then the crucial piece of DNA which contains the HS- RDEB is rapidly copied many times again. This process is called PCR (polymerase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

The genes and proteins that cause HS-RDEB

HS-RDEB is caused by alterations (known as mutations) in the type VII collagen gene found on chromosome number 3. Mutations switch the gene off and so no type VII collagen is made. Type VII collagen is an important protein, holding the different layers of the skin together. Without this protein, the skin is very weak and fragile.

We all have two copies of each gene, one inherited from our father, and the other from our mother. In a child with HS-RDEB, there are mutations in both copies of the type VII collagen gene. The parents of an affected child are both carriers - they have one normal copy of the type VII collagen gene and a mutation on the other copy of the gene (see diagram below).

Diagram to show how HS-RDEB is inherited



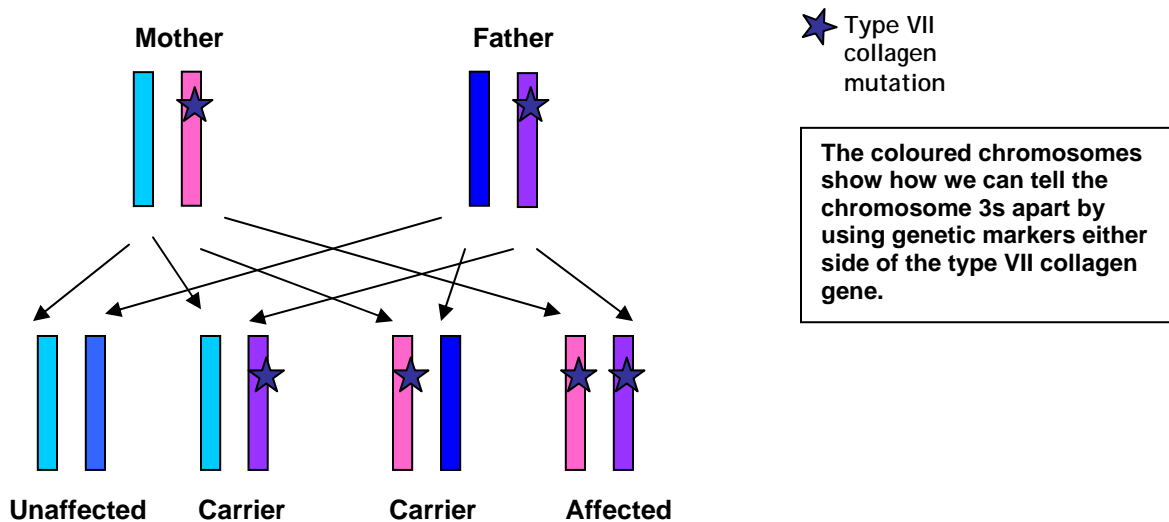
Linkage analysis

The test used for PGD of HS-RDEB involves linkage analysis. This uses the principle of DNA fingerprinting and compares the genetic markers in your DNA samples with genetic markers in the embryos' DNA (see diagram below). This tells us two pieces of information:

- that the cell being tested is definitely a cell from your embryo and not from another source;
- that the test has worked properly and that the DNA from both copies of chromosome 3 has shown up on the analysis and that the embryo has inherited one gene from each parent.

For linkage analysis, we will need a blood sample from each of you.

Diagram to show how linkage analysis works in PGD



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):

- an embryo has two copies of the normal HS-RDEB markers and is **unaffected**;
- an embryo has one copy of the normal HS-RDEB marker and one copy of the affected marker and is **a carrier**;
- an embryo has two copies of the affected HS-RDEB markers and is **affected**;
- the test has failed to produce a result in the embryo.

Only embryos that are **unaffected** or **carriers** will be considered suitable for use.

Accuracy of the test

We take great care to ensure that the diagnosis is as accurate as possible. There is a chance however, that the result in the embryo analysed could be incorrect. Fortunately the chances of this happening are relatively small, around 1% (1 in 100).

Confirmation of diagnosis

As PGD is not 100% reliable, we offer a prenatal test (test in pregnancy) to women who become pregnant following treatment. This test will confirm the diagnosis. It may be a CVS (chorionic villus sampling) done at 11 weeks of pregnancy or an amniocentesis test 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. We will make arrangements to contact you with this result.

Limitations of testing

Testing the embryos is limited to offering a test for HS-RDEB. It is not possible to carry out any other tests on the single cells at the same time, for example Down syndrome. The chances of any other problems affecting your embryos are the same as for any other couple in the general population. The incidence of Down syndrome does increase with a woman's age. You may wish to have a prenatal test for this if you do 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. In the meantime, if you have other questions please ring us on the contact numbers given in the main booklet.

Other useful contacts

DeBRA (Dystrophic epidermolysis bullosa Research Association)

DEBRA House

13 Wellington Business Park

Dukes Ride

Crowthorne

Berkshire

RG45 6LS Tel: 01344 771961 E-mail: debra.uk@btinternet.com

Website: www.debra.org.uk

Amniocentesis: Test done during pregnancy. A fine needle removes fluid from the amniotic sac (water that surrounds the fetus in the uterus) 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.

We have leaflets on amniocentesis and CVS. If you would like copies, please ask a member of staff.

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

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Guys & St Thomas NHS Foundation Trust

