

Preimplantation Genetic Diagnosis Herlitz junctional epidermolysis bullosa 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 the genes that cause Herlitz junctional epidermolysis bullosa (HJEB)

Testing for Herlitz junctional epidermolysis bullosa

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 HJEB gene (either the *LAMA3*, *LAMB3* or *LAMC2* gene) is rapidly copied many times again. This process is called PCR (polymerase chain reaction).

You may remember that HJEB is caused by changes in either the *LAMA3*, *LAMB3* or *LAMC2* genes (found on chromosome numbers 18, 1 and 1 respectively). There are many different types of gene changes and you will know which ones you carry. We all have two copies of the *LAMA3*, *LAMB3* or *LAMC2* genes because most of our genes come in pairs. A child affected with HJEB will have a gene change in both copies of either the *LAMA3*, *LAMB3* or *LAMC2* genes. Their parents will have one normal copy of the gene and one altered copy.

Linkage analysis

As there are hundreds of gene changes causing HJEB, it is not possible to look for each of these gene changes in the embryo cells. Therefore the technique of linkage analysis helps us get around this problem. Linkage analysis uses the principle of DNA fingerprinting and 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 those carrying the altered HJEB gene and those carrying the normal HJEB gene. To do this part of the test, we will need to look at blood samples from you and perhaps other family members.

Linkage analysis tells us two pieces of information:

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

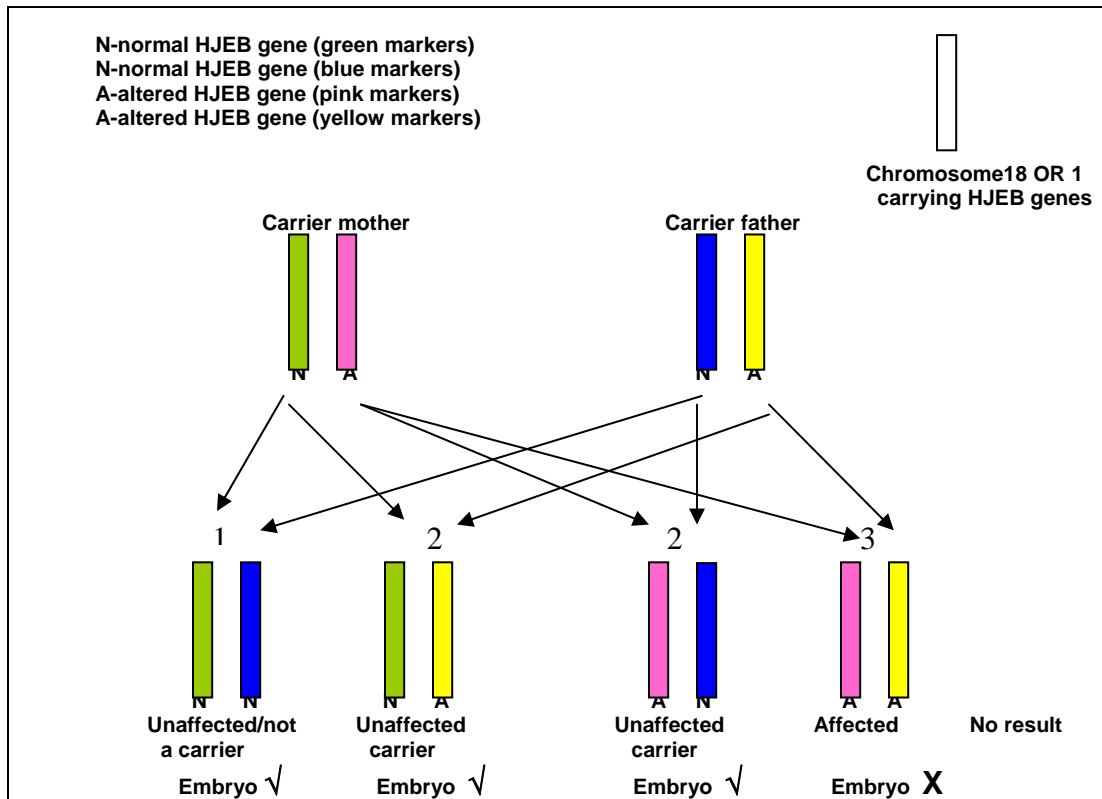
Outcome of testing

Results in your embryos

The results we obtain in each embryo will be one of the following (see diagram below):

1. An embryo has two copies of the normal HJEB gene (**NN**) (green & blue markers) and is **unaffected and not a carrier**.
2. An embryo has one copy of the normal HJEB gene and one copy of the altered HJEB gene (**AN**) (either green & yellow markers or pink & blue markers) and is an **unaffected carrier**.
3. An embryo has two copies of the altered HJEB gene (**AA**) (yellow & pink markers) and is **affected**.
4. 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**.

Diagram to show possible outcomes of PGD



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. This is likely to be approximately 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% 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 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 HJEB. The chances of any other problems affecting your embryos, e.g. Down syndrome, 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 be 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

DebRA UK

DebRA House,

13 Wellington Business Park,

Dukes Ride,

Crowthorne,

Berkshire RG45 6LS

Telephone: 01344 771961

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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.

Guys & St Thomas NHS Foundation

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