

INFORMATION ON GENETIC TESTING AND CONSENT FORM FOR PATIENTS AND FAMILIES WITH DISORDERS OF BLOOD CLOTTING

Disorders of blood clotting can cause bleeding or thrombosis. These disorders may run in families and your healthcare professional will have explained how this affects your family. The purpose of this information sheet is to explain the reasons why you are being offered genetic testing and includes the consent form you will be asked to sign before these are performed.

Genetic tests may answer the following questions:

- If you are known to have a bleeding or thrombotic disorder, what is the genetic change that has caused the condition in your case?
- Are you a carrier of a bleeding or thrombotic disorder?

Introduction

Why do we resemble our parents? How does a single cell grow into a whole human? Genetics is the science that tries to answer these questions. Humans, like every other living creature, are made up of cells. We all start off as one cell at the time of fertilisation. This cell contains two sets of genes, one from our mother and one from our father. These genes are made of a chemical called DNA and each cell holds about two metres of it. For ease of storage and access, the genes in DNA are packaged up into 46 chromosomes. As the single cell divides the genes are copied so that every new cell possesses the full complement of genetic material (DNA).

Humans have approximately 20,000 genes stretched out along their DNA. Each gene acts as the recipe for the production of a protein and together they make up the recipe book or blue print for you and me. Different genes or recipes are read at different times in different cells in response to the requirements of our bodies.

Sometimes genes, like recipes or blueprints, may have spelling mistakes in them or have bits missing. When this happens, the proteins are either not produced or are abnormal. Genes with these mistakes or variants can cause genetic disorders. Since genes are passed on from one generation to the next, genetic disorders often run in families. These mistakes can arise when a cell does not accurately copy its DNA. A mistake or variation in a single DNA letter can lead to disease but some variants have no harmful effects.

Genetic testing can tell us which people in your family have the condition. In some conditions there are individuals who don't show the clinical effects themselves but might pass the disorder on to their own children. These are referred to as 'carriers'. Simple tests of the defective clotting protein can sometimes tell us if a person is affected by the disorder or is a carrier. In carriers these tests are often normal and genetic testing may be the only way of identifying them. With modern genetic testing it is usually possible to locate the faulty genetic change in each family, although this can sometimes take time. Sometimes the same genetic change is seen in unrelated families with the same disorder and sometimes a unique genetic change is found in a particular family.

1. **What is the purpose of obtaining a blood sample?** It is very useful to know what the exact change is in the DNA that is causing the disorder in you/your child. Sometimes this helps us to understand better how the disorder may respond to treatment in the future. Measurement of

the blood clotting factor level or platelet testing does not always clearly indicate if there is a genetic change present or not. Analysis of the DNA is a more accurate way of telling this. For this a blood sample is required from which the DNA can be extracted. A second sample may be taken from you on a separate occasion to confirm the result of the initial test.

2. **Where will the blood sample be tested?** The tests needed to detect a change ('spelling mistake' or bit missing) in DNA are specialised. Some of them are performed locally, but depending upon the nature of the disorder, it may be necessary to send your blood sample away to one of a small number of specialised laboratories. In all these laboratories there are strict regulations in place to ensure complete confidentiality of your details.
3. **How long will the test take?** The answers to genetic tests often take some time to obtain. The healthcare professional explaining the test to you will discuss the likely time course, as this varies with the disorder. It may take several months or years if you have one of the less common or more complicated disorders.
4. **How long will my blood sample be stored?** It is usual practice to store DNA samples indefinitely for several reasons. Sometimes it may not be possible with existing methods to find the genetic change in your family. In this case, the DNA will be stored until new tests are available. Other new tests relevant to the disorder may arise in the future and further analysis of your sample may then be required. Sometimes when testing family members is it useful to have the samples from other family members available for confirmation.
5. **What are the risks of genetic testing?** In addition to information on the inheritance of the disorder that we are testing for, the results from these genetic tests may sometimes inadvertently provide other information about family relationships, such as paternity. If it is found, for example, that an individual's parent is different from that assumed by the family, this may cause significant psychological problems and this may cause harm to the person being tested and other family members.

The studies performed will often be specific for the disorder in your family. These types of tests will not exclude all forms of possible coagulation disorders.

Some genetic testing can be completed using a 'panel'. This is where multiple genes are tested at the same time and is helpful to investigate patients who have an unknown cause for their bleeding or thrombotic condition. If your blood is to be tested using the 'bleeding panel', for example, it is important to know that there are a small number of genes on the panel which are known to be associated with other disorders such as cancer. If a genetic change is found that is known to cause another disorder separate to the one for which the test was done, that is referred to as an 'incidental finding'. Only incidental findings that are considered important for your own health or that of a relative are reported back to your care team. Your healthcare professional will discuss the implications of the test with you prior to you agreeing to a blood sample. If you would prefer not to know about changes in these other genes, you should discuss with your healthcare professional whether there are alternative ways of doing the test.

The results of some genetic tests are inconclusive, which means that we might find a change in a gene but do not know whether it is the cause of a disease. These changes to genes are known as 'variants of uncertain significance' (VUS). As more data accumulate over time, a VUS may be

found to be unimportant and non-disease causing or alternatively may be found to be the cause of a certain disease. If this occurs and your report changes, we will contact you.

6. **What else might be done with my blood sample?** We might want to use your sample to help develop or refine genetic tests for coagulation disorders. In such cases your blood samples would be used in a completely anonymous way so that the results could not be linked back to you.
7. **Who gets to know about the results?** The results will be told to you personally. Your family doctor will be told about the result.
8. **Why might it be useful for other members of my family to know about the results?** Information about the genetic disorder in you/your child is likely to be of benefit to other members of your family. It may, for example, be used to discover if a woman is a carrier and therefore if there is a risk of passing on the disorder to her children. With your permission we would like to be able to make the information about your genetic change available to doctors looking after other people in your family if they ask.
9. **Are my genetic results going to be stored anywhere other than in my hospital and GP case records?** There are local and national confidential databases within the NHS, which keep information about genetic disorders of coagulation. We would like use these to record the information about your gene change. These databases are secure and protected and your personal information will not be sent outside the NHS. In addition to this, anonymised details of genetic variants are stored in international databases so that the results from many people can be evaluated in a co-ordinated manner. This is to improve our ability to interpret genetic variants in the future and to benefit other people who may have a similar disorder.
10. **Will having this genetic test affect my insurance premiums?** No. The Department of Health has agreed with the Association of British Insurers that results from genetic tests that provide information about possible future risk (predictive tests) should not be used to determine premiums except for tests for Huntington's Disease. You should answer all questions on the insurance application form honestly and accurately and include information about your diagnosed blood clotting disorder where asked for.

If you would like to have your blood tested please read and sign the consent form on the next page. If you require further information, or you are unclear about what you have been told, please ask for clarification or more help.



RECORD OF DISCUSSIONS regarding testing and storage of genetic material

I have discussed genetic/genomic testing with my healthcare professional and understand that:

1. Family and wider implications

The results of my test may have implications for me and members of my family. I understand that my results may also be used to help the healthcare of others nationally and internationally, through a process that will not personally identify me.

2. Uncertainty

The results of my test may reveal genetic variation whose significance is not yet known. To decide whether findings are significant for myself or others, my data may be compared in confidential databases to other patients' results across the country and internationally. I understand that this could change what my results mean for me and my treatment over time.

3. Unexpected information and Incidental findings

The results of my test may also reveal unexpected results that are not related to why I am having this test. These may be found by chance and I may need further tests to understand their significance.

4. DNA storage

Normal NHS laboratory practice is to store the DNA extracted from my sample after my current testing is complete. My DNA might be used for future analysis and/or to ensure that other testing, for example, that of my family members, or testing performed at other NHS laboratories is of high quality.

5. Data storage

The data from my test will be securely stored so that it can be looked at again in the future if necessary.

6. Health records

Results from my test and my test report will be part of my patient record.

Note of other specific issues discussed (e.g. specific items not consented to):

I agree to genetic/genomic investigations for the purpose of: (insert reason for test)

Signatures:

Patient/Guardian

Healthcare professional's name

Healthcare professional's signature

Date ____/____/____

Affix sticky label or fill in details

Patient name: _____

Hospital No. : _____

Date of birth ____/____/____