**Topic: Genetic Testing**

# Factsheet

* Genetic testing can be used to find out whether a person is carrying a specific altered gene (genetic mutation) that causes a particular medical condition.
* It may be carried out for a number of reasons, including to:
* diagnose a person with a genetic condition
* help work out the chances of a person developing a particular condition
* determine whether a person is a carrier of a certain genetic mutation that could be inherited by any children they have

**Genes, Chromosomes and DNA**

* Most genetic tests examine DNA (Deoxyribonucleic acid), the chemical in our cells that gives our bodies instructions about how to grow, develop and function.
* DNA is a string of coded messages organised into specific instructions called genes.
* Humans have 30,000 different genes, arranged on a number of thread-like structures, called chromosomes.
* We inherit our chromosomes from our parents, 23 from our mother and 23 from our father, so we have two sets of 23 chromosomes, or 23 ‘pairs’.
* If you think of genetics as the book of life, then the DNA are the letters, the genes are words, and the chromosomes are the chapters.
* Changes in genes or chromosomes are called mutations. You could think of a mutation as a spelling mistake or a series of words changed in a sentence.
* Mutations are very common and we all carry a number of them.
* The effect of a mutation can be good or bad, or it may have no effect at all. This depends on environmental factors, an element of chance, or mutations in other genes.
* Mutations can cause problems if they stop the gene or chromosomes communicating the correct instructions needed for the body to function properly.

**What does genetic testing involve?**

* Genetic tests aim to find mutations in a particular gene or chromosome.
* Testing usually involves having a sample of your blood or tissues taken. The sample will contain cells containing your DNA.
* A sample is taken from the patient and sent off to the laboratory so that the genes or chromosomes can be analysed.
* It can be tested to find out whether you’re carrying a certain mutation and are at risk of developing a particular genetic condition.
* In some cases, genetic testing can be carried out to find out whether a baby is likely to be born with a certain genetic condition.
* This is done by testing samples of the fluid that surrounds the foetus in the womb (amniotic fluid) or cells that develop into the placenta (chorionic villi cells), which are extracted from the mother’s womb using a needle.
* Depending on the condition(s) being checked for, the fluid or cell samples will be examined and tested in a genetics laboratory to look for a specific gene, a certain mutation on a specific gene, or any mutation on a specific gene.
* In some cases, it may be necessary to check an entire gene for mutations using a process called gene sequencing.
* Depending on the specific mutation being tested for it can take weeks or even months for the results of genetic tests to become available.
* It isn’t always possible to give definite answers after genetic testing. Sometimes it’s necessary to wait to see if the person being tested, or their relatives, do or don’t develop a condition.
* It is also worth remembering that a genetic test will usually only provide information about the condition that was tested for.
* There is no general test for all genetic conditions.
* The aim of a genetic test done at the genetic clinic is to provide information about the health of the individual or family. Genetics clinics do not usually order tests for other issues, such as to check paternity, although information about this may sometimes be revealed in the course of testing.

# 2. DNA Sequencing Diagram



# 3. Genetics Laboratories

There are two main types of genetics laboratories. One looks at genes and one looks at chromosomes.

**1) Cytogenetics**

If a doctor suspects a genetic condition is caused by a problem on one of the chromosomes, they will ask a cytogenetics laboratory to examine the patient’s chromosomes. Samples taken from blood, skin or the material obtained from amniocentesis and CVS tests can be used. First the cells are grown. The cells are then put onto microscope slides and the chromosomes are stained with a dye so that it is easier to see them.

The cytogeneticist will first check the number of chromosomes. Some conditions are caused because there are additional chromosomes. One of the most common examples of this is Down syndrome. People with this condition usually have one additional chromosome in their cells. The cytogeneticist will also check the structure of the chromosomes. Changes in chromosome structure happen when the material in an individual chromosome is broken and rearranged in some way; it may involve the addition or loss of chromosome material. These changes can be so small that they can be hard to detect. Sometimes a different technique known as Fluorescence In-Situ Hybridisation (FISH) is used to detect changes that are too small to be seen under the microscope or to double check a small change seen under the microscope.

Cytogenetic testing can be a lengthy process. The laboratory first need to grow cells and this takes at least a week. It can then take another week or so to prepare the slides and analyse the chromosomes one by one under the microscope.

**2) Molecular genetics**

If a doctor suspects a genetic condition which is caused by a change (mutation) in a gene, they will ask a molecular genetics laboratory to examine the DNA of a particular gene. The instructions within the DNA are written out as a code made up of four letters: A, C, G and T. The molecular genetics laboratory can examine the precise sequence of the code in a particular gene to see if there are any errors, or spelling mistakes if you like. A single gene, however, may consist of 10,000 or more letters of DNA code. So, a molecular geneticist’s skills lie in being able to read through the code and find the changes. If these changes cause the gene not to give the correct instructions to the body, this can cause a genetic condition.

Unlike chromosomes, DNA cannot be seen under a microscope. The molecular geneticist extracts DNA from the cells and uses the DNA to perform specific chemical reactions to read the code of the gene of interest. Many different techniques are used to detect mutations. Checking the sequence of DNA is one commonly used method.

**How does a laboratory know if a mutation is harmful?**

This is a very important question. Genetics laboratories have a saying that ‘anyone can find a mutation, but not everyone can interpret them’. Mutations can have different degrees of seriousness and knowing what effect a mutation will have requires expert knowledge of the disease and the gene or chromosome, and attention to detail. So how does a laboratory know whether a mutation is good, bad or has no effect at all?

First of all it is critical that an expert, such as a clinical geneticist, has looked at the patient, their relatives and their family history, and perhaps also the results of any other investigations carried out. This gives the geneticist clues about what gene or chromosome to investigate. So, if for example the geneticist thinks the patient may have cystic fibrosis because the patient is showing symptoms of the condition, and other family members have had the condition, they will take a sample from the patient and send it off to the laboratory for testing. They will provide the laboratory with all the relevant information about the patient and their family history and tell them to look for one of the mutations that causes cystic fibrosis, then they know that the patient has this condition.

In some cases, a child is affected by a condition but neither of the parents has the mutation. In this case it is likely that the mutation has happened for the first time when that bay was conceived. This is called a ‘de novo’ (from the Latin) or ‘new’ mutation.

In some cases, a laboratory may not know whether a mutation is disease-causing or not. This may be because the change in the DNA code is very subtle. These mutations are called ‘unclassified variants’ and receiving this result can be frustrating for all involved. However, it is extremely important that a laboratory does not say that a mutation is harmful when it is not as this might lead to someone being given an incorrect diagnosis.

Can laboratories always find mutations?

In some situations, a test is carried out to find the cause of a problem and no mutation is found.

There are a number of reasons as to why this is:

* sometimes a genetic test will only look at the most common mutations that cause a particular condition. If the patient has a very unusual mutation the laboratory may therefore not find it.
* scientists have not identified all the genes that cause genetic conditions.
* the patient may not have the condition they appear to have, and therefore the scientists may not be looking in the right gene.

It is important to remember that genetic testing techniques and our knowledge of genetics is advancing rapidly. Therefore, even if a mutation cannot be found now, there is still a possibility that new techniques will enable scientists to find it in the future.

**Why do some genetics tests take so long whilst others can be done quickly?**

If the laboratory knows exactly what mutation it is looking for, because somebody else in the family has the same condition, or because the laboratory knows which area of the gene to look at, it has a much easier task. The test may then take only a week or two.

However, if no mutation has previously been found in the family, or if there are a number of genes associated with the condition, it will need more work to get a result. Instead of focusing on one area of a gene the lab may need to analyse the whole gene or even more than one gene. This can be a very long process and can take many months. This will depend on a number of factors such as how big the gene is and the facilities available at the laboratory.

For example, in the case of Duchenne muscular dystrophy, the condition is cause by mutations in a gene called dystrophin, one of the longest genes known. There are thousands of different possible mutations that can occur, and therefore finding a family’s particular mutation can be a very long ad laborious process. On the other hand, in the case of Huntington’s disease, mutations in the huntingtin gene always occur in the same small region. Therefore, the scientist knows exactly where to look in the gene and so the test is fairly easy and much quicker.

The quality of the DNA is also an important factor. Sometimes laboratories first have to check the DNA of someone who is deceased in order to identify the particular mutation. If the DNA from the deceased person is poor quality, this can double or triple the time it takes to find the mutation. In some cases it may not be possible to complete the analysis because there is not enough DNA.

**(Source:**<https://www.nhs.uk/Conditions/Genetics/Documents/What%20happens%20in%20a%20Genetics%20Laboratory.pdf> )

# 4. Chief medical officer calls for gene testing revolution

**By Michelle Roberts, Health editor, BBC News online**

Cancer patients should be routinely offered DNA tests to help select the best treatments for them, according to England's chief medical officer.

Prof Dame Sally Davies says in her annual report that the NHS must deliver her "genomic dream" within five years.

Over 31,000 NHS patients, including some with cancer, have already had their entire genetic code sequenced.

Dame Sally wants whole genome sequencing (WGS) to become as standard as blood tests and biopsies.

**Personalised medicine**

Humans have about 20,000 genes - bits of DNA code or instructions that control how our bodies work. Tiny errors in this code can lead to cancer and other illnesses.

Sometimes these mistakes are inherited from a parent, but most of the time they happen in previously healthy cells.

WGS - which costs about £700 - can reveal these errors by comparing tumour and normal DNA samples from the patient.

Dame Sally says that in about two-thirds of cases, this information can then improve their diagnosis and care.

Doctors can tailor treatments to the individual, picking the drugs mostly likely to be effective.

And WGS can also show which patients are unlikely to benefit, so they can avoid having unnecessary drugs and unpleasant side-effects.

**Quicker diagnosis**

Dame Sally wants DNA testing to become standard across cancer care, as well as some other areas of medicine, including rare diseases and infections.

"I want the NHS across the whole breadth to be offering genomic medicine - that means diagnosis of our genes - to patients where they can possibly benefit," her report says.

People with rare diseases could benefit from having greater access to the technology, speeding up diagnosis.

Doctors are already using genetic tests to identify and better treat different strains of the infectious disease tuberculosis.

Dame Sally said patients could be assured that their genetic data would be stored securely and "de-identified" so that their privacy would be protected.

**The Genomic Dream**

Over 10 years ago, international scientists reached a breakthrough in DNA work - sequencing the entire genetic blueprint of man. The Human Genome Project meant experts now had a catalogue of DNA code to explore and refer to.

They began to understand which genes controlled which processes in the body and how these could go wrong.

Doctors then started to "read" a patient's DNA to get a better idea of what might be causing their symptoms and how best to treat their illness.

Genomic medicine - tailoring care based on an individual's unique genetic code - is now transforming the way people are cared for by the NHS.

Genes can predict if a woman with breast cancer might respond to certain drugs, or whether radiotherapy is likely to shrink a tumour, for example.

Currently, genetic testing of NHS patients in England is done at 25 regional laboratories, as well as some other small centres.

Dame Sally wants to centralise the service and set up a national network to ensure equal access to the testing across the country.

A new National Genomics Board would be set up, chaired by a minister, to oversee the expansion and development of genomic services.

**Sensitive data**

Dame Sally told BBC Breakfast that a lot of money was being spent because it was currently operating like a "cottage industry".

By having centralised laboratories, more could be done with the money, including keeping up with the latest technology, she said.

She said one hurdle could be doctors themselves, who "don't like change", and she urged cancer service patients to press their doctors to move from a local to a national service.

She also said patients must understand they needed to allow use of their data, alongside other data, in order to get the best diagnosis, and therefore the best treatment.

Phil Booth, from campaigning organisation, MedConfidential, said this move had "huge potential" for patients and the NHS, but there were "great risks with large collections of sensitive data".

"Every single use of patient data must be consensual, safe and transparent," he told BBC Radio Four's Today programme, and patients should be able to opt-out if they so wish.

(<https://www.bbc.co.uk/news/health-40479533>)

1. **Questions**

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| 1. What is DNA?
2. What are genes?
3. What are chromosomes?
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| 4. What are the main reasons genetic testing is used? |
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| 5. What is a mutation and how can it cause a problem? |
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| 6. What does genetic testing involve? |
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| 7. What does a mutation look like in a sequence of DNA? |
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| 8. Describe the two types of genetics laboratories. What is the difference between the two? |
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| 9. How does a laboratory know if a mutation is harmful? |
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| 10. Why do some laboratories not always find mutations? |
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| 11. What does Prof. Dame Sally Davies want the NHS to do? What is her argument for this? |
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| 12. What do you think the main pros and cons of genetic testing are? |
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