

be reassured that the most up-to-date testing is available. Laboratories may use anonymised DNA samples to help develop new tests, or share them as part of Quality Assurance (QA) schemes, unless an individual specifies that they do not wish their sample to be used in this way. Like any stored clinical samples, DNA is regarded as part of a patient's medical record and is therefore kept in medical confidence. This means that access to it is only possible through an appropriate health-care professional.

Some people are concerned about the police accessing their DNA. This is an extremely rare request. If the police should want access to a DNA sample from the genetics laboratory (as with any other part of a patient's medical record), this is only possible on production of a court order.

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March 2009

This work was supported by EuroGentest, an EU FP6-supported NoE contract number 512148.

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# What Happens in a Genetics Laboratory?



## Information for Patients and Families

## What Happens in a Genetics Laboratory?

The following information describes what happens to a sample when it is sent to the genetics laboratory. The main points discussed are:

- The different methods used in the laboratory to perform genetic tests.
- Why some genetic tests take so long whilst others can be done quickly.
- Why in some cases the laboratory cannot find a result.

For detailed information about why you might take a genetic test, please look at the leaflet called ***What is a Genetic Test?***

### Section 1: What is a genetic test?

Most genetic tests examine **DNA**, 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.



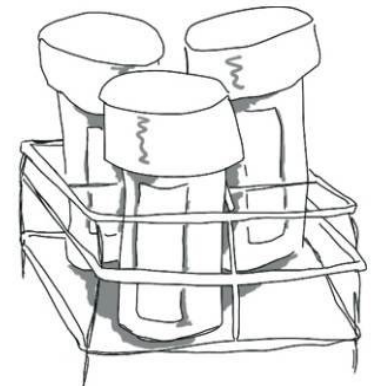
## Can the results be wrong?

Because genetic tests have very important implications for an individual and their relatives, they are treated very carefully. Numerous steps are taken to ensure that the correct result is given. If a mutation is found it is always double-checked to ensure that the result is correct (although machines are used during many parts of the test, a scientist will still always check the results). Often, scientists will perform another test to 'cross-check' the first result. Procedures are also in place to make sure that samples do not get mixed up. Additionally, many laboratories take part in Quality Assurance (QA) schemes, which helps ensure that they perform good quality, reliable genetic tests.

### What will happen to my sample once the test has been done?

Unless a patient requests that their sample be discarded after testing, a laboratory will usually store the DNA, and may store chromosome samples. Laboratories will be happy to let you know about your sample, and individuals can request at any time that their DNA be destroyed or returned to them. Testing for other conditions is not performed without consent from the patient.

As new improved tests are developed, laboratories may perform these tests on stored samples (if, for example, initial testing did not provide any results), if consent has been given. In this way both patients and clinicians can



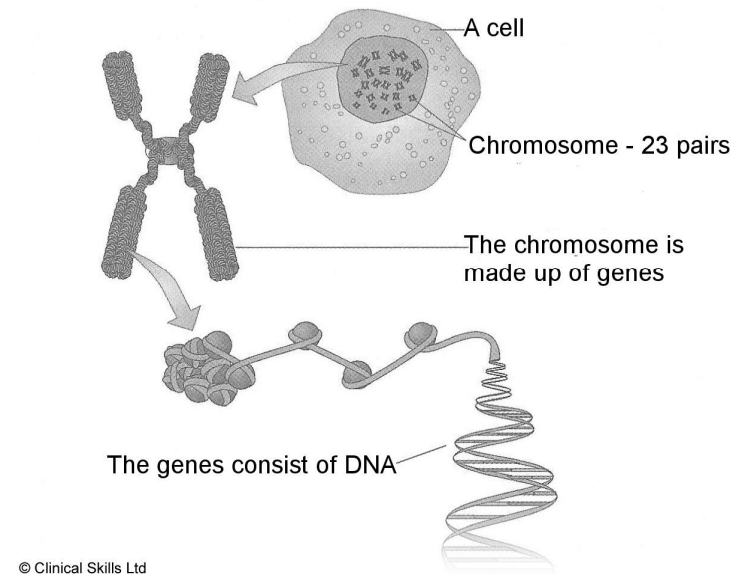
because somebody else in the family has the same condition or because the laboratory knows which area of the gene to look at, it has a much easier task. The test may then take only a week or two.

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 caused 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 and 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 scientists know 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.

**Figure 1: Genes, chromosomes and DNA**



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 chromosome communicating the correct instructions needed for the body to function properly. Genetic tests therefore aim to find mutations in a particular gene or chromosome. The tests are usually performed on blood or sometimes other tissues. (In some cases it is possible to take a saliva sample to get DNA. However, usually the scientist will need a good amount of high-quality DNA, so a blood sample is preferred.) A sample is taken from the patient and sent off to the laboratory so that the genes or chromosomes can be analysed.

Genetic clinics usually have their own genetic laboratory. However, because there are so many genetic tests for so many different conditions, not all laboratories perform every test. This is particularly the case for tests for the rarer genetic conditions. Therefore, the sample may be sent to another laboratory that specialises in the particular test that the doctor wants performed.

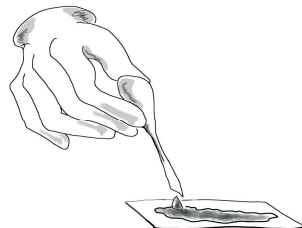
It is also worth remembering that a genetic test will usually only provide information about the condition that was tested for. There is no general test for all genetic conditions. The aim of a genetic test done at the genetic clinic is to provide information about the health of the individual or family. Genetic 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.

## Section 2: Genetics Laboratories

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

### 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.



know whether a mutation is disease-causing or not. This may be because the change in the DNA code is hard to interpret. 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 genetic tests take so long whilst others can be done quickly?

If the laboratory knows exactly what mutation it is looking for,

## 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 the mutations that cause cystic fibrosis. If the laboratory finds two cystic fibrosis mutations, one on each chromosome, then they know that patient has cystic fibrosis.

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 baby was conceived. This is called a 'de novo' (from Latin) or 'new' mutation.

In some cases a laboratory may not



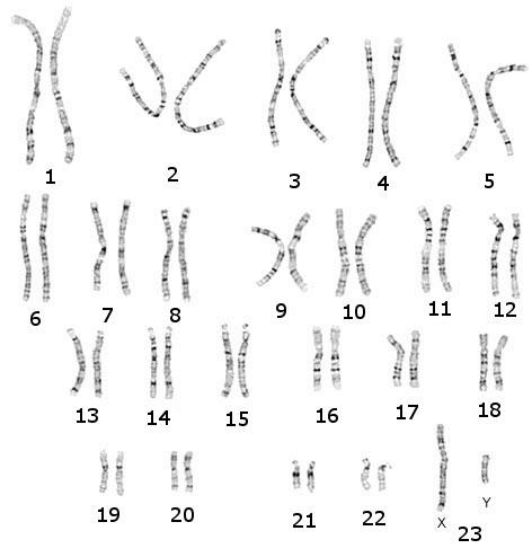
## Figure 2: How the chromosomes appear under the microscope



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's 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.



**Figure 3: Chromosomes after they have been arranged in order: a karyotype**



Cytogenetic testing can be a lengthy process. The laboratory first needs to grow the 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.

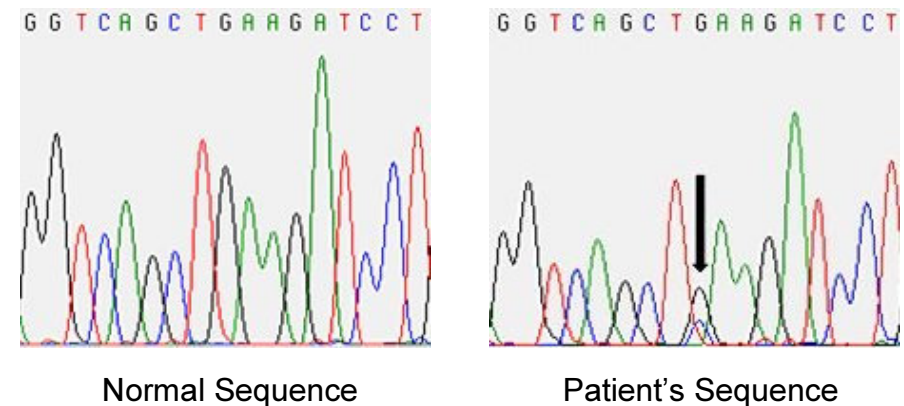
### Molecular genetics

If a doctor suspects a genetic condition that 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 skill lies 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.

**Figure 4: DNA sequencing: spot the difference!**



Here is a short stretch of code from a gene. If you can see the image in colour then you will see that each letter of DNA code is displayed in a different colour. The picture on the left shows the normal sequence, and the picture on the right is from a patient. In the picture on the left each letter has a single 'peak'. However, in the picture on the right you can see that this patient has two 'peaks' at the same position, a G (black line) and a C (blue line). This shows that there is a mutation at this point, on one of the chromosome pairs.