Genetic Tests for Health Purposes

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We have all inherited a unique combination of genes from our parents. This original constitution and the influence of various environmental factors throughout life explain the differences between one person and another in terms of appearance, sensitivity to certain types of treatment, susceptibility to diseases, etc.

Scientific advances are enabling us to explore the human genome and glean information from it. Any laboratory test conducted with a view to obtaining information on specific aspects of the genetic status of an individual is a genetic test.

It is important to remember that for the vast majority of conditions, your genes only partly influence your risks of developing them. Factors such as your medical history, your lifestyle and your environment also play an important role.

This information document is geared to providing general information on genetics and its influence on our health, as well as guidance on how to approach genetic testing.

Under what circumstances is genetic testing foreseen?

A genetic test conducted in a medical framework can provide information which is important for a person's health. There are various medical reasons for genetic testing. If your physician thinks you might have a disorder with a genetic component, he/she may refer you to a duly qualified physician, who specialises in investigating, diagnosing and treating individuals who are suspected of having, or who do actually have, a genetic problem. The background to your disorder will be carefully considered, as well as any personal and family precedents and your symptoms. If a specific genetic disorder is suspected, a genetic test will be proposed, if available, with a view to establishing a definite diagnosis.

The need for professional genetic counselling

Because of the possible serious impact of genetic testing, people who are considering taking a genetic test are strongly advised to seek genetic counselling. This is provided by specially trained professionals and involves objective information that will help you and, where appropriate, your family to take a decision. Genetic counselling will take into account your situation and needs and will provide you with information on all the options that are available to you, without trying to influence your decision.

Genetic counselling services may also involve professional psychological support before and, if you should decide to take a genetic test, after the test to help you deal with the implications of the test results. This support may include communicating and explaining the results of the test to family members. Genetic counselling therefore supports individuals before, during and after the genetic test.

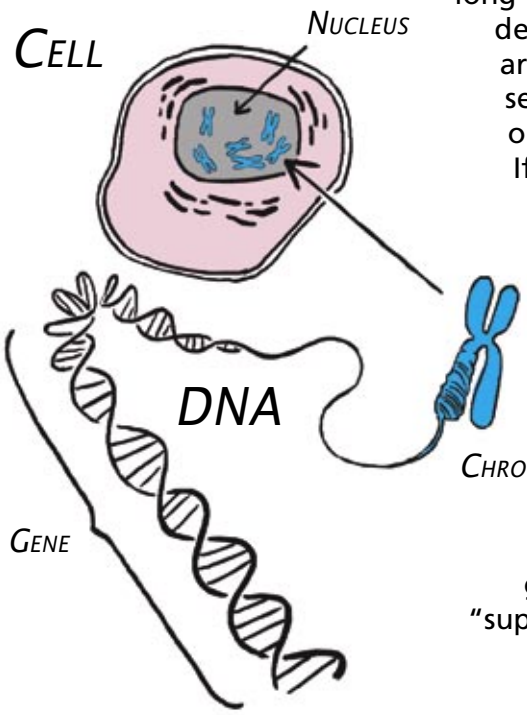
Some common reasons for considering a genetic test:

- You or your child have symptoms of a disorder and you want to make a diagnosis or find a biological cause responsible for the disease
- A genetic condition runs in the family and you want to know if you are at risk of developing this condition during your lifetime
- A genetic condition runs in the family or you belong to a group or population in which there is an increased risk of a specific genetic condition, and you want to know whether you might pass this condition to your children
- You or your partner has had several pregnancies which did not go to term.

▪▪▪ Some biology...

Every human body has several trillions of cells, the basic building blocks of all living creatures. Cells provide structure to the body. They convert nutrients in foodstuffs into energy and carry out various specialized functions. Cells of the same type combine to form tissues, which in turn combine to form organs. There are over 200 different types of cells making up the muscles, nerves, lungs, heart, sexual organs, blood, etc.

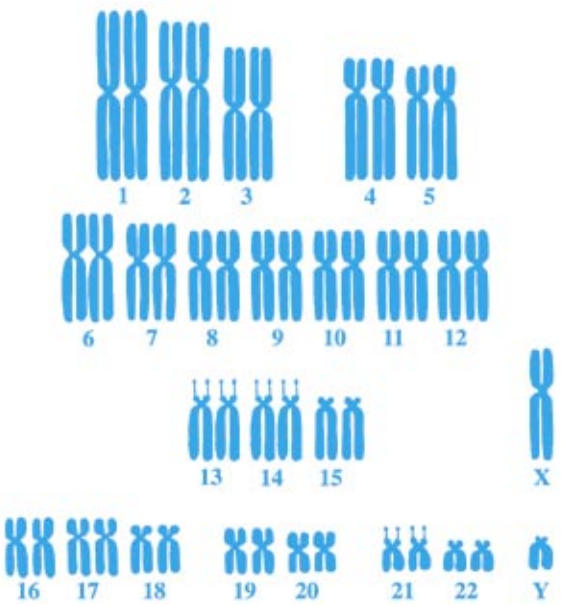
Most cells have a nucleus in which all the necessary information for the development and proper functioning of the organism is stored. The items of information are "written" in a biological support called DNA (deoxyribonucleic acid). If DNA is like a long sentence providing a complete description of an organism, genes are like separate words within this sentence. A gene is involved in one or more functions in the organism. If it is damaged or deficient it can no longer properly carry out this function. The whole set of genes forms the genome.



A cell nucleus thus contains the genome, which is the person's "genetic make-up". Every child receives half of his or her genome from each parent, which is why the genome is often referred to as the "support of heredity".

What about chromosomes?

Mainly composed of DNA, chromosomes are only visible during cell division. Human beings have 46 chromosomes, or 23 pairs to be exact, because chromosomes come in pairs: one pair of sex chromosomes – called X and X for female, X and Y for male – and 22 pairs of non-sex chromosomes, numbered from 1 to 22.



What is a genetic test looking for?

A genetic test is an analysis of part of your DNA. A genetic test can help determine if there is a change in a particular gene or chromosome. The change, often referred to as mutation, may affect all the cells in the organism and be transmissible to future generations.

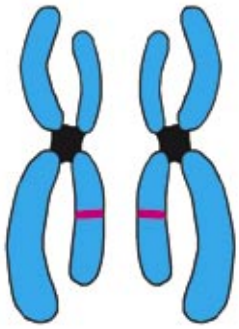
Your genes and your physician

In order to study DNA, first a blood or saliva sample is taken and sent to a laboratory for testing. The lab generally gives the test results in writing to the physician who prescribed the test, who will then discuss them with you.

There are three main types of disorders resulting from genetic mutation:

- Chromosomal disorders

Chromosomal abnormalities occur when a person has one or more damaged chromosomes (e.g. crossover on chromosomes or missing part of chromosome), or when the person does not have 46 chromosomes. This is the case in individuals with Down's syndrome, who have an extra copy of chromosome 21, giving a total of 47 chromosomes.



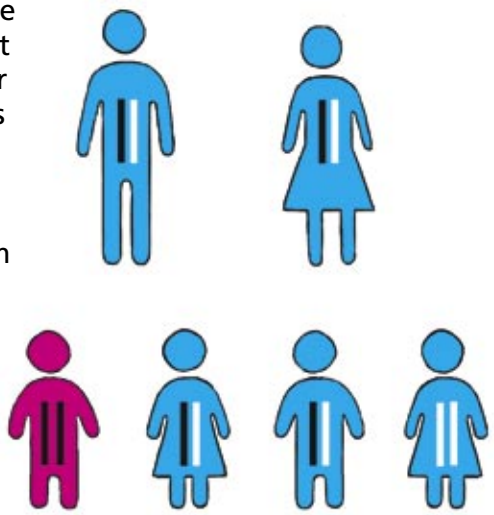
Chromosomes with two alleles of the same gene

- Monogenic disorders

Monogenic disorders are the result of a change in a single gene. Monogenic disorders are usually severe and rare, although they still affect millions of people worldwide. The nature of the disorder depends on the functions performed by the mutated gene. All human beings have two copies – the scientific term is "allele" – of each gene. One allele comes from the father and the other from the mother.

Some monogenic disorders are linked to the alteration of a single allele. This is the case for Huntington's disease, a disease that affects muscle co-ordination and cognitive functions.

Other monogenic disorders only develop when the two alleles are altered. Individuals with only one altered allele do not develop the disease but merely carry the mutation. This is the case for cystic fibrosis, a chronic disease which affects the lungs and the digestive system. When only one allele is altered, the persons concerned are not sick, but carrier of the mutation. They are known as (healthy) carrier. Carriers seldom have any symptoms of the disorder, but if two carriers have a child together, there is a 25% chance that the child will inherit two mutated copies of the gene and therefore will develop the disorder.



■ Complex genetic disorders

Complex genetic disorders are the result of the interaction of several gene alterations in combination with environmental factors and lifestyle. Complex genetic disorders include very common diseases such as diabetes, most cancers, asthma or heart disease. Unlike in the case of monogenic disorders, many genes are involved in the onset and development of this kind of disorders.

Although it is an important focus of genetic research, the genetic component of common disorders is still poorly understood and tests concerning complex genetic disorders are considered to be inaccurate or indeed irrelevant predictors of the potential development of a disorder.

The different types of genetic tests

> Diagnostic genetic tests

Diagnostic genetic tests are intended to diagnose a genetic disorder in a person who already has symptoms. The results of this test may help to make choices about how to treat or manage health problems. They may also help solve the problem of diagnostic uncertainty, enabling individuals at last to know from what disorder they are suffering.

> Predictive genetic tests

Predictive genetic tests are performed on individuals who show no symptoms as yet. They are geared to detecting genetic changes which suggest a risk of developing a disorder later in life. This probability may vary substantially from one test to another. In rare cases, the genetic test would give an indication of a high probability of developing a condition later in life (e.g. Test for Huntington disease).

In most cases, the test would only provide an indication of a risk of developing the disorder during your life, but will not be an accurate predictor because environmental factors play an important role next to genetics. Such predictive tests are referred to as susceptibility genetic tests.

> Carrier tests

Carrier tests are used to identify people who 'carry' a mutated allele of gene which is associated with a specific disease (e.g. cystic fibrosis). Carriers may show no signs of the disease. However, there is a risk that their children will be affected.

> Pharmacogenomic tests

Pharmacogenomic tests are performed to test individuals sensitivity to a specific therapy. For example, some individual might need higher dosage while others may display an adverse reaction to certain medications.

Potential benefits of genetic testing

- For some specific conditions, a genetic test may provide certainty about your or your child's disorder. For some people putting an end to uncertainty is very important.

- A genetic test may help diagnose a genetic condition and lead to treatment (when available) or preventive measures (when available).

- The results of a test may provide useful information for future pregnancies.

- As genetic disorders are often hereditary, information on your genetic characteristics may be useful for other members of your family.

Limitations and possible risks of genetic testing

- Taking a genetic test, waiting for the results, and then receiving them may cause a range of mixed emotions such as stress, anxiety, relief or guilt. It is important to consider the possible consequences for you and your family if you were to receive either good news or bad news.

- Even though a diagnosis may be confirmed by genetic testing, intervention or treatment is not always available.

- It may not always be possible to secure a genetic explanation for a specific condition, for various reasons: the test may not yet be available, or it may not have been developed because the genetic basis has not yet been identified.

- For some conditions in which a genetic basis has been identified as having caused the condition, it is not possible to tell how severely a person will be affected.

- The results of your genetic test may reveal genetic information about other members of your biological family – with whom therefore you share some genetic characteristics - in particular with regard to their genetic risk of a condition. Will other family members want to know this information?

- Test results may sometimes reveal family secrets involving paternity and adoption.

■■■ Your decision to take a genetic test

This decision can be a difficult one to take. It is a personal choice. Everyone is free to choose whether to request a genetic test or not, and also whether to be informed of the results of the test or not. It is therefore important that you are provided with very clear and complete information and that you have been able to ask all the questions you wish, so as to remove any shadow of a doubt before taking a decision.

Genetic testing in children

Genetic testing in minors has always been approached cautiously. Usually, children and adolescents will only be genetically tested if urgent preventive or therapeutic measures depend on the test result. In case testing is not urgent (e.g. the onset of the disorder occurs only in adulthood and no therapy can be initiated before that time) testing is usually postponed until the minor is old enough to make an informed choice himself/herself.

You should ask various questions before deciding to take a genetic test:

- About the disorder:
  - What do we know about the disorder?
  - Is everybody with this disorder affected by it in the same way?
  - What might it be like to live with this disorder?

- Why do I or my child have this disorder?
- Are other family members at risk for this disorder?
- Is there any treatment for this disorder?
- If so, can I have access to it?
- Where can I find more information about the disorder?

▪ About the test:

- Are there risks in taking the test? If so, which are they?
- What will the results of the test tell me?
- How accurate will the test result be?
- Do other members of the family need to be tested?
- How long will it take before I get the test results?
- Who will give me the test results?
- Who will have access to the test results?

The results of a genetic test are sensitive personal data concerning your "biological privacy". They are therefore to be considered as confidential.
Moreover, people who have taken a genetic test are strongly advised to seek support (genetic counselling) to ensure proper understanding of their meaning and implications.

▪ Other relevant questions:

- Will the results of the test have consequences for other members of my family?
- If so, should I discuss the test with them first?
- What might be the emotional impact of the results on me and my family?
- Who should I tell about the test results?
- Will I get written information about what we have been discussing?
- Who can help me explain the results to my child and/or relatives, if I so wish?
- Are these results liable to be transmitted to other persons? If so, to whom?
- Are there any support services or patient organisations I can contact?
- What other health professionals should I get in contact with?

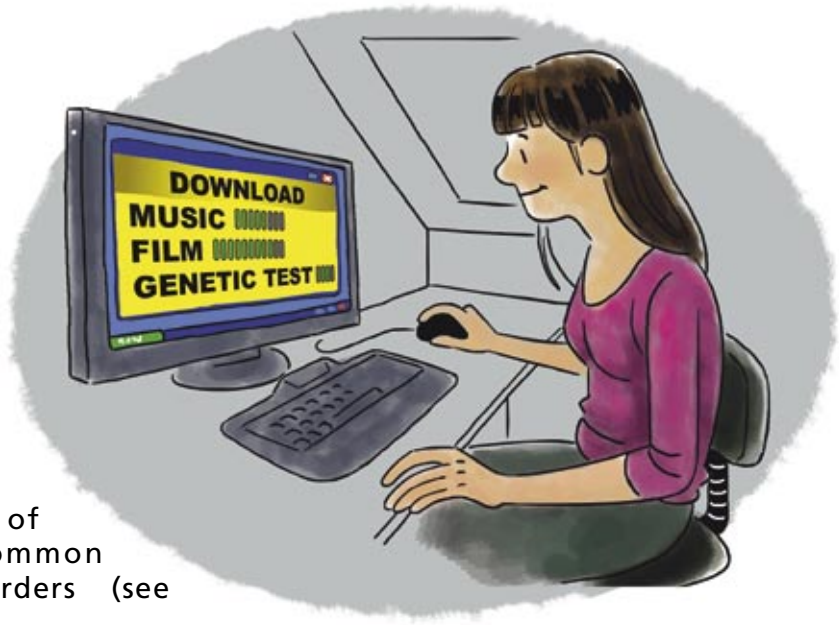
▪▪▪ Direct-to-consumer genetic testing

In recent years, there has been an increase in the number of genetic tests advertised and/or sold through the internet by societies outside the established healthcare system.

What are these companies?
In fact, the many companies who sell these tests let you buy them over the internet in the same way as for buying books or CDs. Most of these companies have been advertising and offering genetic testing services often without any involvement from a healthcare professional.

What can be tested for?

The tests sold by these companies include some of the well-validated tests your doctor can offer, but they also offer many more tests that have not yet been validated or are deemed inappropriate to offer to the public. Most companies sell genetic tests that are supposed to estimate your risk of developing certain common complex genetic disorders (see above).



Things you should know about genetic tests sold directly-to-consumers:

- Many genetic tests being sold directly-to-consumers are not considered to be valid by the health care system. This means that the quality and utility of the tests have not been proven. Most test results are not able to predict whether you will develop a certain disease or how severe this disease might be. As was already underlined above, for the vast majority of conditions, your genes only partly influence your risks of developing them. Other factors such as your medical history, your lifestyle and your environment also play an important role.

- Ordering a genetic test is not the same as ordering a book. It is always important to first consider the possible consequences for you and your family if you were to receive a test result.

- Genetic testing on children is always to be considered with great caution (see box Genetic testing in children). It is strongly advised not to carry out genetic testing on children outside established health care systems.

- Many companies operate without medical supervision and without a direct patient-physician interaction. Talk to your doctor about whether this test might provide useful information about your health. Make sure you understand the benefits and limits before you buy a test.

- Ask what will happen with your sample and how the privacy of your sample and information will be safeguarded. Ask whether your information will be shared with other companies or research organisations.

- If you have ordered a direct-to-consumer genetic test, discuss with your doctor before making health-related decisions.

More information on genetic testing:

- www.eurogentest.org/patient/

EuroGentest has developed a series of leaflets to provide general information for patients and families about genetics and genetic testing.

- www.orpha.net

Orphanet provides databases about rare diseases, orphan drugs, expert centres, diagnostics tests, patient organisations, ...

What this document is about

This information document aims at providing general objective information on genetic tests, including their nature and the potential implications of their results. It presents the different type of test available, their applications in the medical field and the extent and limit of the significance of the information resulting from these tests.

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