

HEREDITARY TESTING

Cancer and blood diseases in children

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01 INTRODUCTION

This brochure provides you with information about hereditary testing in children and teenagers who have recently or in the past been diagnosed with cancer or a blood disease.

02 HEREDITARY TESTING: WHAT AND FOR WHOM?

Why hereditary testing?

Generally the development of childhood cancer is not hereditary. In 5 to 10% of children and teenagers with a tumour or blood disease, an underlying hereditary predisposition does play a role. The Center for Medical Genetics (CMGG) uses DNA testing to determine whether a child got the disease as the result of a hereditary predisposition.

The CMGG team consists of a clinical geneticist, a psychologist and a nurse. They give genetic advice tailored to the family and discuss the possible outcomes of hereditary testing for the child and his/her family members.

A genetic consultation consists of:

- ▲ No-obligation confidential genetic counselling and DNA testing
- ▲ Recommendations for screening and/or treatment based on possible DNA test results
- ▲ Voluntary participation in scientific research

How is hereditary testing carried out?

Hereditary testing is generally based on a blood sample. In some blood diseases we need to remove a small piece of skin (= skin biopsy). This is generally done at the same time as another procedure or treatment under general anaesthetic. We often also ask for a blood sample from both parents. This simplifies the interpretation of the test. Using these samples, we investigate whether we can find a hereditary predisposition for your child's disease.

03 GENETIC CONSULTATION

Why may it be useful to identify a hereditary predisposition?

- ▲ Paediatricians can provide tailored follow-up, including risk assessment for the future, a personalised follow-up plan and screening.
- ▲ Other family members may be genetically tested to see if they too have an increased risk of a tumour or blood disease. If this is the case, they can receive extra monitoring and protection.
- ▲ We can usually prevent the hereditary predisposition from being passed on to future children.

The first consultation

The consultations are multidisciplinary: both the clinical geneticist and the psychologist are present. The first consultation lasts 45 minutes to an hour.

During the appointment, the doctor will discuss your child's medical history. We also make a family tree to chart the medical history of your relatives as best we can.

The following topics are covered:

- ▲ The medical history of the child, the parents and other family members.
- ▲ Specific conditions that increase the likelihood of a hereditary disease.
- ▲ Timing: is there added value in starting hereditary tests of the child now?
- ▲ How hereditary testing is carried out: which tests, duration, sampling.
- ▲ The possible consequences for the child and screening recommendations if a hereditary predisposition is identified.
- ▲ The impact of hereditary testing on other family members.
- ▲ Your expectations around hereditary testing.
- ▲ Your attitude and that of other family members towards the hereditary test.
- ▲ The emotional impact of hereditary testing.
- ▲ Opportunity to participate in scientific research if you want.

The clinical geneticist will also examine your child during this consultation. If you want, you can also come without your child the first time. We will then schedule the clinical examination at another time, for example when your child is on the nursing ward.

Preparation for the first consultation

For the first consultation, you and your child register at the registration kiosks at entrance 11. As a parent, it is necessary that you yourself are also registered so that a blood sample can be taken during the consultation.

We need to know as much as possible about the medical history of family members such as parents, brothers and sisters, grandparents, aunties and uncles. If one of them is or was ill, it is useful for us to know the correct diagnosis:

- ▲ Has a (close) family member had a tumour or blood disease? Then we would like to know at what age the diagnosis was made and what type of disease your family member had.
- ▲ Has a (close) family member had tumours in a number of body parts? Then we would like to know if it was one type of cancer that spread (metastases) or different types that developed independently of one another.
- ▲ Has a (close) family member already had genetic testing carried out? Then it is useful for us to see the report, provided that your family member gives permission for this.

Whether to have a hereditary test or not

The first consultation is informative. You will be given plenty of time to decide for yourself whether or not you want to have a hereditary test carried out on your child.

- ▲ Some families decide to start genetic testing fairly quickly. Sometimes we can already take a sample at the first genetic consultation.
- ▲ Other families opt to leave this for a while and to have genetic testing carried out at a later stage in the treatment process. If this is what you want to do, we agree where and when the sample will be taken. We schedule this into the treatment plan so that your child does not have to make an extra visit to the hospital.
- ▲ If you decide not to start hereditary testing (for the moment), you can contact our centre yourself again later when you do want to start.

04 HEREDITARY PREDISPOSITION TO CANCER

There is a hereditary predisposition in some families. This can sometimes be indicated by the following characteristics:

- ▲ A number of relatives have a similar tumour or blood disease.
- ▲ The tumours or blood disease were diagnosed in these family members at a relatively young age (often before the 50th birthday).
- ▲ Clinical examination indicates specific characteristics in the child.
- ▲ With certain kinds of tumours there is a high probability of an underlying hereditary predisposition.

05 RESULTS

We estimate that in about 5 to 10% of the children, their diagnosis indicates a hereditary cause. The following results may be obtained from genetic testing:

Your child has a hereditary predisposition for certain tumours or blood diseases

This diagnosis enables us to make a better estimate of the likelihood of new tumours and the places in the body where they may occur. Paediatricians monitor your child closely (screening) to increase the chances of identifying any new tumours at an early, curable stage.

- ▲ A hereditary predisposition can **arise spontaneously**. The likelihood is then very small that brothers and sisters, parents and/or other family members have the same predisposition.
- ▲ The predisposition can also be **inherited**. Brothers, sisters, parents and/or other family members may also be a carrier of the predisposition. Therefore, they too are eligible for genetic testing and customised screening. In adult carriers who want to have children, we can use reproductive techniques (e.g. IVF) to prevent them passing on the predisposition to the next child.

No hereditary predisposition is found

This is reassuring. There is very little chance that family members will develop a similar condition.

Variations with unclear meaning

DNA changes are interpreted based on current scientific knowledge. Sometimes it is unclear whether a change in a gene is part of the normal variation that makes us all different or is responsible for the disease. Sometimes additional testing can help shed more light on these variations. If this is not possible, we do not report the DNA change.

06 HOW DO YOU GET THE RESULT?

The doctor who requested the test receives a DNA report from the Center for Medical Genetics. We never give out results by telephone or email.

If you opt for genetic testing, we schedule your next consultation at the Center for Medical Genetics. If a sample has already been taken, we arrange a consultation with the clinical geneticist once the results are known.

The DNA report is generally available after four to six months.

07 DESIRE TO HAVE CHILDREN

With reproductive techniques such as in-vitro fertilisation (IVF) and embryo selection, we can prevent a couple becoming pregnant with a child who inherits the hereditary disease of which the parent(s) is/are a carrier. We call this technique pre-implantation genetic testing or PGT.

In PGT we make the genetic diagnosis on a number of cells from embryos that have developed in vitro. Only the embryos that do not carry the hereditary predisposition are eligible for transfer into the womb.

At the Center for Medical Genetics we can provide you with detailed information on this option so that you can make an informed choice.

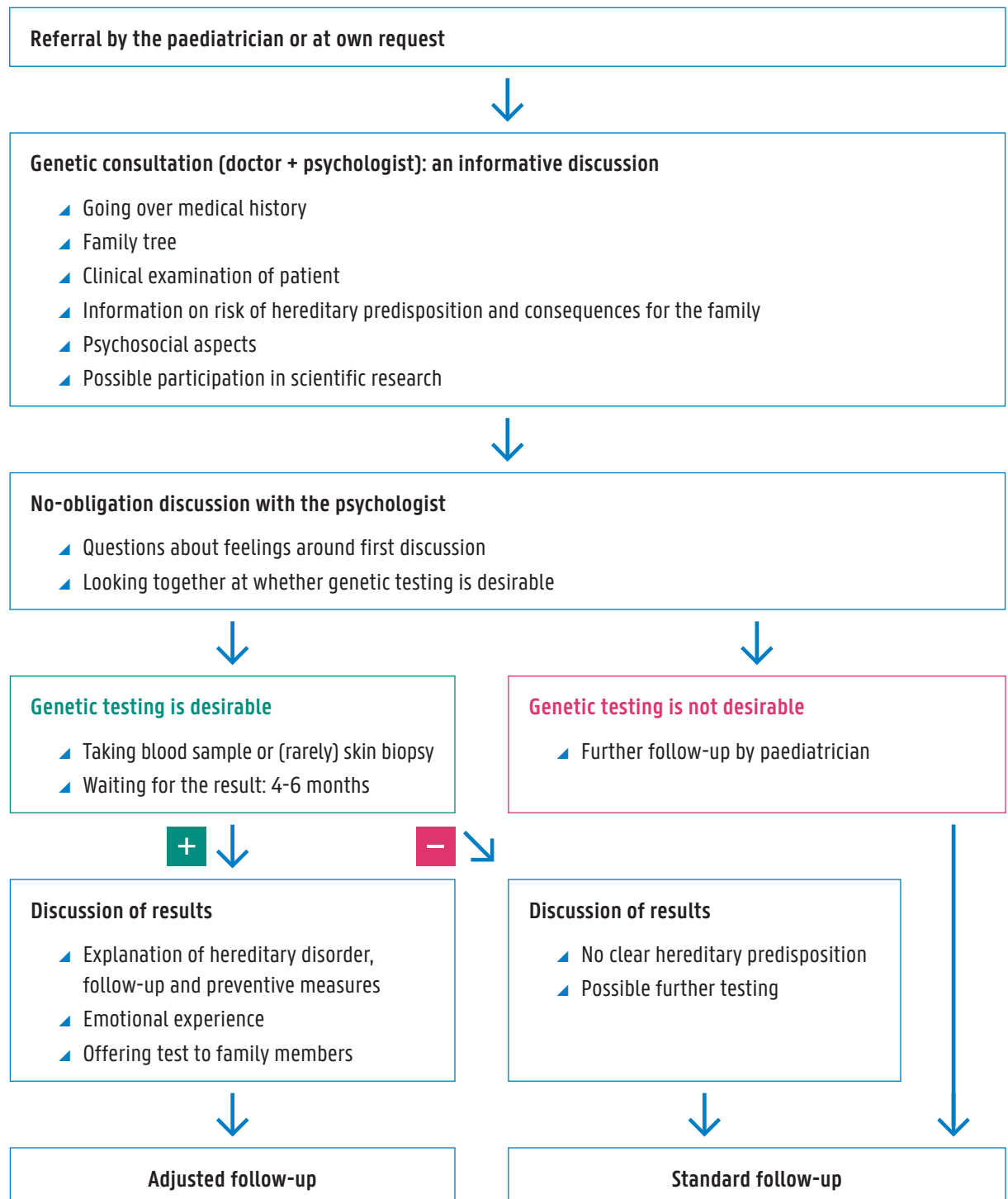
08 PSYCHOLOGICAL SUPPORT

People at risk of a genetic disorder are sometimes worried. Uncertainty may also affect other family members or relatives. We provide psychological counselling and follow-up. We can also schedule additional discussions. We take the time to discuss your questions and concerns and those of your child.

09 COST

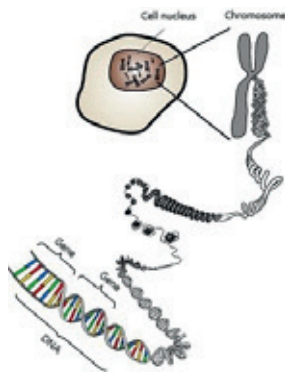
Genetic testing is reimbursed by the National Institute for Health and Disability Insurance (RIZIV). The own contribution is limited to 8.68 euros per genetic test.

10 GENETIC TESTING STEP BY STEP



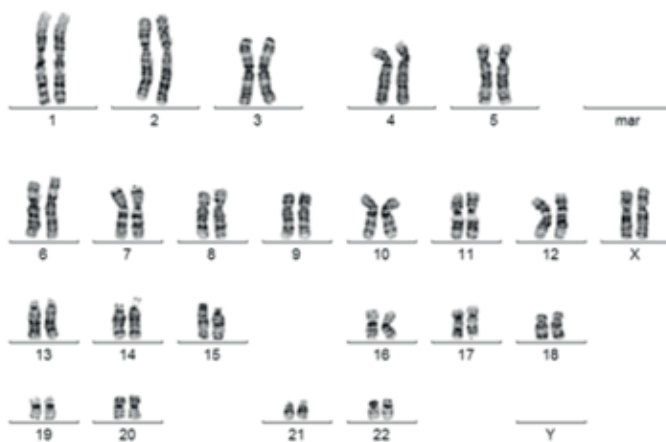
11 HEREDITY

The hereditary material or DNA is located in the nucleus of each cell in our body and is packaged into chromosomes. Genes are located on these chromosomes and these genes contain a kind of code for all our hereditary characteristics. They tell our cells how they must develop and how they must function and determine, for example, the colour of our hair and eyes. Changes in our genes make us all a bit different. Most changes are harmless. But some changes cause the gene to stop working normally, which then results in a disorder: we call this a mutation. This kind of mutation can cause a person to develop a hereditary disorder.



Chromosomes

Chromosomes ensure that DNA is stored in a compact manner. We have two copies of each chromosome: one copy comes from the mother and one copy comes from the father. For this reason we also have two copies of almost all our genes. There are two basic types of chromosomes: the autosomes (non-sex chromosomes) and the sex chromosomes. The sex chromosomes determine the sex. A man has one X and one Y chromosome (XY), a woman has two X chromosomes (XX). All autosomes and sex chromosomes together make up the DNA, also called the genome.



Example of a female chromosome map

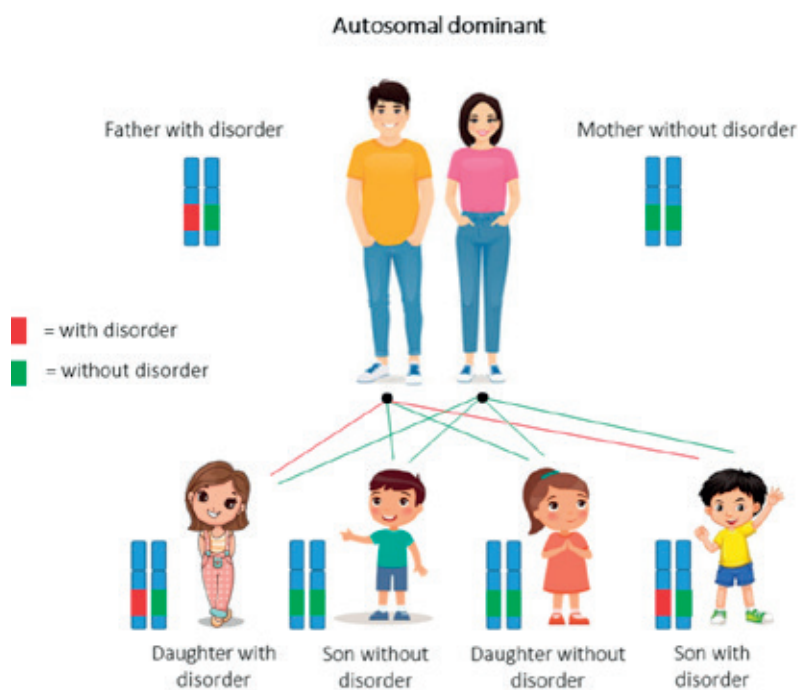
Monogenic disorders

Disorders that are caused by a mutation in a single gene are called monogenic disorders. These monogenic disorders can be autosomal dominant, autosomal recessive or X-linked, where autosomal means that the gene in question is on one of the 22 non-sex chromosomes:

Autosomal dominant disorder

A disorder is dominant when a mutation in one of the two copies of a gene results in the disorder. These mutations may occur again at fertilisation (*de novo*), but may also be inherited from a parent.

If one of the parents carries this kind of mutation, in every pregnancy there is a 50% chance of this mutation being passed on. Carriers of mutations in specific genes may have an increased risk of certain tumours or blood diseases.

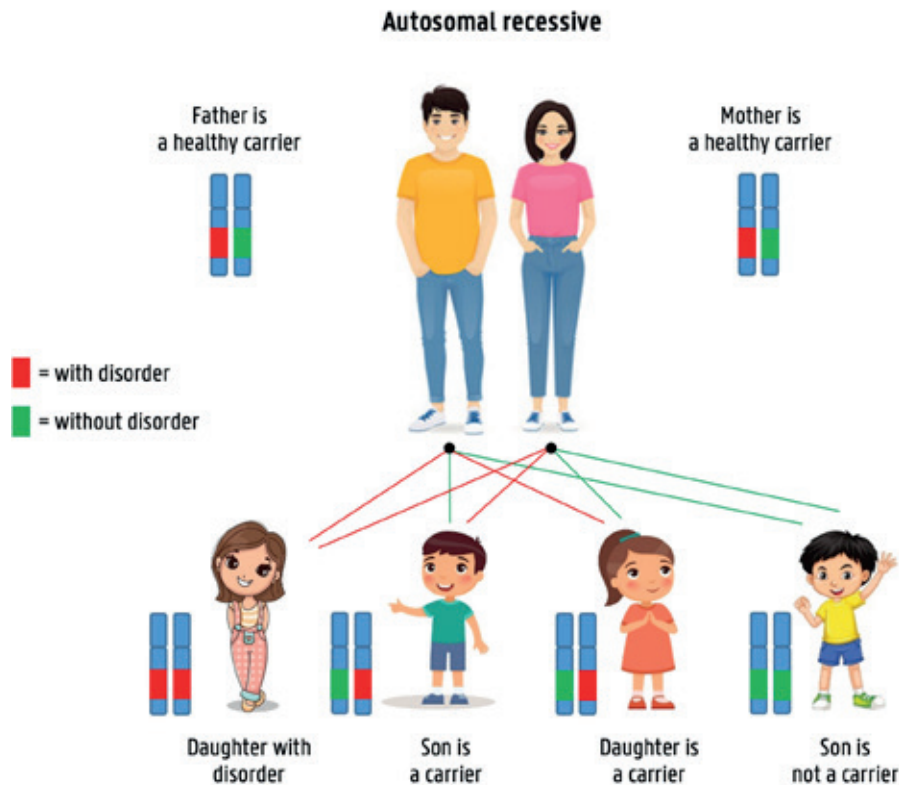


Most hereditary predispositions are inherited in an autosomal dominant manner. If there is an autosomal dominant disorder in the family, we often see that several family members get cancer at a relatively young age.

Autosomal recessive disorder

A recessive disorder occurs when a mutation is present in both copies of a gene. A person who carries a mutation in only one of the two copies of a recessive gene is usually a healthy carrier.

When both parents are carriers of a mutation in the same autosomal recessive gene, together they have a 25% chance of having a child with the disorder in each pregnancy. The parents are generally both healthy carriers.



A minority of hereditary predispositions are inherited in an autosomal recessive manner. Because carriers of an autosomal recessive mutation are generally healthy, people with the same disorder rarely occur in the family. However, siblings have a 25% chance of having the same hereditary disposition.

X-linked inheritance

An X-linked inheritance of a tumour predisposition is rare. Usually only boys/men have an increased risk. Sometimes the disorder may occur in both boys and girls, but is more pronounced in boys.

12 CONTACT

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13 THE TEAM



From left to right:

- ▲ **Marie Van Poucke** (nurse consultant paediatric haematology and stem cell transplantation)
- ▲ **Sophie Van Hoyweghen** (psychologist, PhD student)
- ▲ **Prof. dr. ir. Kathleen Claes** (laboratory manager Center for Medical Genetics)
- ▲ **Prof. dr. Bram De Wilde** (paediatrician haematology/oncology and stem cell transplantation)
- ▲ **Dr. Robin De Putter** (clinical geneticist Center for Medical Genetics)
- ▲ **Dr. Charlotte Derpoorter** (researcher paediatric haematology/oncology and stem cell transplantation)
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- ▲ **Dr. Sabine Hellemans** (psychologist Center for Medical Genetics)