

Information for patients about sickle cell disease and/or thalassemia

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1. What is sickle cell disease?

A substantial part of our blood is made up of red cells (erythrocytes) These are responsible for carrying oxygen. The red blood cells contain a red-coloured pigment called hemoglobin which picks up oxygen in the lungs then takes it around the body. This is usually hemoglobin A. In people with sickle cell disease this red pigment is slightly different and is called hemoglobin S. Their red cells change shape when there is a shortage of oxygen. Then the cells get the shape of a sickle. Only by examining the blood the diagnosis of sickle cell disease (or sickle cell anemia) can be made.

2. How do you get sickle cell disease?

Sickle cell disease began in Africa and that is still where it is most commonly found. However, the disease is found in people all over the world. It can be passed on from parent to child. The genetic material (DNA) of those with sickle cell disease differs slightly from that found in people without the disease. Sickle cell disease in a person develops only if both parents pass on the defective genetic material. Sickle cell disease is **an inherited disease**. It is **not infectious**, and cannot be caught from blood of someone with the disease (e.g. from a blood transfusion).

3. How are the symptoms of sickle cell disease caused?

Because the red blood cells are different a number of problems occur:

I. Sickle cells are broken down by the body faster than normal cells.

For this reason there are fewer red blood cells and a condition called **anemia** occurs. The symptoms of anemia are: becoming tired very easily, listlessness, no energy and a buzzing noise in the ears. The rapid breaking down of the red blood cells causes a yellow pigment (*bilirubin*) to be released. This gives the skin and eyes a yellow colour and is called **jaundice** (icterus). People with sickle cell disease are more vulnerable to infection. In infection the breakdown of the blood cells becomes even faster and causes a number of symptoms: suddenly becoming very pale and more jaundiced, the urine becomes dark (it looks like cola), heart palpitations, dizziness, faintness and shortness of breath. This is called an **anemic crisis**.

II. The red blood cells begin **sickling** (changing shape) when:

1. The cell is offered not enough oxygen: its store is very small and gets used up quickly. This can happen high up in the mountains or during aeroplane flights if the cabin is not pressurised.
2. The body needs a lot of oxygen e.g. during great physical exertion (sport played at a high level or for a long period of time), if there is infection, overtiredness or a shortage of sleep.
3. The body is dehydrated (not enough fluid).
4. The outside-temperature is very low.

The red cells become misshapen and change into rigid sickle shapes which hook onto one another forming a clump of sickled cells. These clumps of cells get stuck in the very small blood vessels and stop the bloodflow. In this situation various organs of the body are unable to get enough blood. This is called a **vaso-occlusive crisis (blocked blood vessels)**. The symptoms that this type of crisis cause depend on in which part of the body the blood vessels are blocked. This can happen in:

*The Bones:

Severe pain in the bones of arms and legs or the back (small children often have pain in their hands and feet). It begins very suddenly and may last for days. It may stay in the same place or jump to another area (e.g. from knee to elbow). Swelling and redness of the skin and tissues of the effected area may occur. This is called a **painful bone crisis** (small children often develop the **hand-foot syndrome**).

*The Lungs:

Suddenly occurring and continuous breathlessness and tightness of the chest may indicate a blockage in the lungs. This is called a lung **infarction**.

***The Gut:**

Suddenly occurring and continuous pain in the belly may indicate a blockage in the gut. This is called a **bowel infarction**.

***The Brain:**

If the brain does not get enough blood the following symptoms may occur: suddenly not able to talk properly, arms and legs feel powerless, or show impaired perception, fits. This is called a **brain infarction or CVA**. Other symptoms of reduced brain function can also occur at some time or another such as: not being able to think clearly, concentration problems or a poor memory.

***The Kidneys:**

Because of the small size of the blood vessels in the kidneys, clumps of sickled cells can get stuck here and can cause **problems of kidney function**: and blood in the urine passing a lot of urine (because the kidneys cannot concentrate it).

This increases the chance of dehydration (not enough fluid in the body) and is especially dangerous during bouts of diarrhoea and fever.

***The Penis**

Sometimes a clump of cells can block the vessels which take the blood from the penis. This can cause a long-lasting painful erection or one which keeps coming back. This is called **priapism**.

***The Eyes:**

The blocking of a blood vessel in the eye can cause deterioration in eyesight.

4. What are the signs and symptoms of sickle cell disease?

The majority of people with sickle cell disease don't have symptoms all year round. They are in a stable phase. Sometimes there are periods of serious illness: **the crises**. Symptoms are caused not only by the disease but also by something as simple as a common cold. In order to distinguish between the different causes we have divided the symptoms into two groups. In the case of symptoms from the second group (Serious acute symptoms) appearing, it is advisable to consult your doctor. Some people feel their crises coming on. Don't wait too long, contact your doctor or go the Casualty (Eerste Hulp) Department at your hospital.

Common Symptoms

- * Easily tired, no energy, listless
- * Slight yellow coloration of the eyes
- * Passing a lot of urine
- * Slow growth in children (due to anemia)

Serious Acute Symptoms

- * Fever (temperature higher than 38.5°C for longer than 24hrs)
- * Headache, powerless feeling or impaired perception in arms or legs, fits
- * A painful crisis
- * A sudden increase in paleness or jaundice (anemic crisis), with or without sudden swelling of the spleen
- * Swollen painful hands and feet (hand-foot syndrome)
- * Suddenly worsening eyesight
- * Sudden breathlessness or tightness of the chest
- * Sudden pain in the high right-hand side of the belly causing inability to either sit or lie down. This could mean gallstones.
- * Painful erection of the penis
- * Passing blood in the urine
- * Leg ulcers

If any one of these **serious acute symptoms** occurs you **must always** contact your doctor or the Casualty Department of your hospital!

5. Learning how to avoid getting the symptoms

In order to avoid getting the symptoms it is important to live according to the following rules:

* Live a healthy life:

- eat a varied diet
- get enough rest
- take enough exercise but don't overdo it (no professional or long lasting sport)

* Avoid stress:

- get enough sleep
- avoid stressful situations
- don't get overtired

* Avoid infection:

- good hygiene
- brush your teeth well and see the dentist regularly (always tell you have sickle cell disease)
- call the doctor if your temperature is higher than 38.5'
- children up to 12 years of age should take penicillin (Broxil) every day in order to avoid infection
- above the age of 12, always have Broxil available at home
- aside from the normal vaccinations such as DTTP, HIB & MMR, vaccination with Pneumovax is strongly recommended. (the first at the age of 2 to 3 years and then repeated when indicated every 5 years)

* Avoid dehydration:

- drink a lot of fluid, especially in hot weather, if you have a fever, diarrhoea or if you are vomiting

* Avoid getting too cold:

- dress warmly in winter, avoid swimming in cold water
- after swimming have a warm shower and dry off quickly

6. How is sickle cell disease inherited?

You only inherit the disease if both parents carry the sickle cell gene with its defective DNA.

Concerning sickle cell disease we can divide people into three groups:

- * Healthy people (they have only normal hemoglobin i.e. hemoglobin A). This group is called **AA**.
- * Carriers of sickle cell disease (they have partly normal hemoglobin A and partly sickle cell hemoglobin i.e. hemoglobin S). This group is called **AS**.
- * Sufferers of sickle cell disease (they only have sickle cell hemoglobin). This group is called **SS**.

Carriers:

Because they have partly normal hemoglobin, carriers suffer almost no symptoms. Problems occur only under abnormal and extremely stressful conditions such as running a marathon at a high altitude. Carriership is also called 'sickle cell trait'.

Carriers can pass on the disease to their children (see examples 1,2 and 3), even though they themselves are not really ill.

The only way to see if someone is a carrier is to do a blood test.

Sufferers:

Every inherited characteristic has two parts: one from the mother and one from the father. A sufferer of sickle cell disease has inherited this characteristic both from mother and father. Both parents must be carriers (example 2), or both sufferers or one a carrier and the other a sufferer (example 3).

To explain more clearly how sickle cell disease is inherited we will give a few examples. Please bear the following points in mind:

- * The examples given are true for **each** child that is born. One sick child does not mean that the next child will be healthy and vice versa.
- * The terms father/mother are interchangeable in every example.
- * Healthy means: not a carrier and not a sufferer.

Example 1:



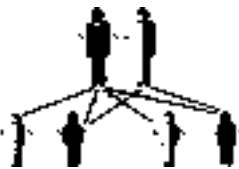
Father is the carrier (AS), mother is healthy (AA). The chance of having a child that will be a carrier is 50%. The chance of having a healthy child is also 50%. No children will have sickle cell disease.

Example 2:



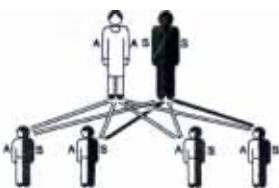
Both parents are carriers (AS). The chance of having a child who will be a carrier is 50%. The chance of having a child with sickle cell anemia is 25%. The chance of having a healthy child is also 25%.

Example 3:



The mother is a sufferer (SS), the father is a carrier (AS). The chance of having a child who is a carrier is 50%. The chance of having a child with sickle cell disease is also 50%. There is no chance of having a child who is healthy and no carrier.

Example 4:



The father is a sufferer (SS), the mother is healthy. The chance of having 0 child who is a carrier is 100%. There is no chance of having a child who is healthy and no carrier.

7. Pregnancy

Women with sickle cell disease often have problems during pregnancy. The anemia becomes more serious and the crises occur more frequently and are more severe. For this reason it is absolutely essential that the expectant mother sees the doctor very often during pregnancy. Usually during the last part of pregnancy a number of blood transfusions are given. Despite the extra care, there is a higher chance of miscarriage. The birth must take place with utmost care in the hospital.

8. Going to the dentist

It is important to tell your dentist that you have sickle cell disease. Infections of teeth or gums can bring on a crisis so good dental and mouthcare are essential. No special measures are necessary during dental procedures such as extracting teeth.

9. Having an operation

During an operation under general anaesthesia cells tend to sickle more quickly. Before an operation it is usually necessary to have one or more blood transfusions in order to prevent sickling. The anaesthetist must also know that you have sickle cell disease.

10. When to contact your doctor?

It is advisable to find a doctor who specializes in sickle cell disease such as a hematologist/pediatrician (children's doctor who is a specialist in diseases of the blood) or a hematologist/internist (a specialist in diseases of the blood and internal medicine). It is advisable that people with sickle cell disease should have a physical check-up once or twice a year at the out-patient's department. Any complication of the disease will then be discovered earlier. You can also ask for advice and information during these visits. If you are suffering from any of the acute, serious symptoms (see Chapter 4) it is vital that you contact your doctor **immediately**.

11. How is sickle cell disease treated?

The cause of sickle cell disease (i.e. the defective inherited gene) is not yet treatable. What we can do is to try and keep in top of the symptoms and help to avoid them.

There are a number of ways of doing this:

1. Antibiotics: to avoid and fight infection
2. Pain killers and extra fluids: for pain in the bones, lungs or belly
3. Folic Acid: to help in making blood
4. Blood transfusions: in cases of severe anemia or painful crises and in cases of lung or brain infarction or at operations
5. Admission to hospital: in cases of very serious, painful crisis, anemia or infection.

12. What does the future hold for sickle cell disease patients?

In the United States, Great Britain and The Netherlands many researchers and doctors are currently working on sickle cell disease.

They are working on:

- * Providing good and complete information to all concerned with sickle cell disease i.e. sufferers and their families, doctors, nurses, midwives, teachers etc.
- * Diagnosing the disease at an early stage
- * Testing new methods of treatment
- * Changing the DNA in the defective gene

13. Heredity

People's hereditary characteristics (such as hair colour, blood group, skin colour, eye colour etc.) are recorded in **genes (DNA)**.

We each have two copies of almost every gene, one of which comes from our mother and the other from our father. So each gene is present **in duplicate**. In this way, the individuals of each succeeding generation pass on half of their genes to each of their children. So one of each pair of genes is passed on. The actual genes that an individual passes on vary from child to child. This explains why children resemble their parents and why siblings resemble one another. But it also accounts for any differences. Each of us carries genes with adverse properties. Some of these result in hereditary diseases, which can occasionally be quite severe, but **the other gene** in the pair often alleviates the symptoms almost completely. Such individuals are referred to as **carriers** and, in the case of blood diseases such as sickle cell disease and thalassemia, these carriers are said to have a '**trait**'.

Will carriers eventually develop anaemia? Although carriers may sometimes suffer from slight anaemia, they are usually entirely free of disease symptoms. In the course of time, carriers do **not** go on to develop full-blown thalassemia or sickle cell disease. Anyone who needs further information about heredity and disease can order a booklet from the Erfo centre of the VSOP (Association of Collaborative Parent and Patient Organizations). For further details, see the section entitled 'addresses' at the back of the brochure.

14. Heredity and prevention

Sickle cell is a hereditary disease. If you have sickle cell disease then **it is certain** that your father and mother are carriers or that they suffer from the disease itself. If your child has sickle cell disease then **it is certain** that you and your husband or wife are either carriers of this disease or suffer from the disease itself. This fact has two major consequences.

a Increased risk of sickle cell disease with each pregnancy

In the case of a subsequent pregnancy there is an **increased** risk that the child will have sickle cell disease. If it is known exactly what type of carriers you and your partner are, then it will be possible to find out how severe your child's sickle cell disease may be.

In some cases, it is possible to carry out tests during pregnancy (or subsequent pregnancies) to determine whether the child in the uterus also has sickle cell disease. This can take place at a very **early** stage of pregnancy, when your period is about 6 weeks overdue.

If a severe form of sickle cell disease runs in your family, you may decide to have an abortion. If so, you should contact your family doctor or your local centre for clinical genetics.

b Family study

If you are a carrier of sickle cell disease or if you suffer from the disease itself, it is certain that this hereditary factor occurs in your family. Your children, parents, brothers and sisters, cousins, uncles and aunts may all be carriers.

In their own interests, it is important that they have themselves tested (to see if they are carriers) before they have children. This is because any of their present or future children will also be at greater risk of sickle cell disease. If necessary, they can also have themselves tested at an early stage of pregnancy.

15. What is thalassemia?

Thalassemia (thalassemia major or Cooley's anaemia) is a severe form of anaemia that can develop in children whose parents are both carriers of thalassemia. While sickle cell disease involves a change in the structure of haemoglobin, in thalassemia one of the components of haemoglobin is **synthesized in inadequate amounts**. About 6 months after birth, a baby with Cooley's anaemia will start producing insufficient amounts of haemoglobin and, as a result, it will develop severe anaemia.

Treatment

The only possible treatment involves **regular blood transfusions**, together with the **administration of medicines** to remove the excess iron that is introduced into the body by these numerous transfusions. Another approach that is currently used, provided that a suitable donor is available, is the use of **bone-marrow transplantation**. However, it is by no means certain that such treatment will be successful.

The transfusions and anti-iron-accumulation treatment must be carried out under close medical supervision. This is necessary to maintain the amounts of haemoglobin and iron in the blood at constant and optimum levels, and to deal with any side-effects and complications. Some of the possible side-effects are enlargement of the liver and spleen, bone abnormalities, growth retardation, disruption of normal development during puberty and of sexual functions, thyroid gland abnormalities, diabetes, infections, and oral hygiene problems.

The attending specialist must take all of these possible side-effects into account.

There are also other types of thalassemia (such as alpha-thalassemia), but they will not be dealt with here.

16. Heredity and thalassemia

Thalassemia is also a hereditary type of anaemia. It is inherited in exactly the same way as sickle cell disease (see section 6). If two partners are both carriers, then they can pass their harmful haemoglobin characteristics on to their children. Each of this couple's children has a 25% chance of inheriting the harmful characteristic from both parents, making them 'double carriers'. Any such children will be severely ill.

In addition, there is a 50% chance that a child will be carrier, just like its parents, and a 25% chance that the harmful characteristic will not be inherited. These children will be healthy.

In theory, anyone in the Netherlands can be a carrier of thalassemia or sickle cell disease, but these conditions very rarely occur in northern Europeans. Such characteristics are more commonly seen in individuals from southern Europe and the countries bordering the Mediterranean Sea, such as Greece, Italy, Turkey, the Middle East and North Africa (Morocco, Tunisia, Egypt etc.). In addition, they are often encountered in individuals from Central Africa, Surinam and Asia (Indonesia, China, Thailand, etc.).

17. Prevention of thalassemia

It is important for everyone, especially young people who want to start a family, to find out whether or not they are carriers of thalassemia (or of sickle cell disease). If blood tests show that someone is a carrier of such a characteristic then, before they have any children, it is vital that they find out whether their partner is also a carrier. This is because, if they are both carriers, there is a 25% chance that their children will have severe thalassemia (or sickle cell disease).

Family studies

If someone is found to be a carrier, it certainly makes sense that a family study be carried out. This is because their brothers, sisters and cousins may also be carriers, which means that their children may also be at risk.

Testing during pregnancy

As with sickle cell disease, it is also possible to test for thalassemia during pregnancy. Parents who are both carriers can, if they wish, make use of such tests to find out whether their child will have the disease. Such tests are carried out at centres for clinical genetics, after the parents have been fully informed about what is involved.

Testing during pregnancy is by means of amniocentesis, when the mother's period is 6 weeks overdue. If the type of thalassemia in the family is one of the more severe forms of the disease and if the results of the test are unfavourable, then the pregnancy can be terminated (abortion) at the parents' request.

18. Some useful addresses

Some addresses of specialists

Amsterdam Academisch Medisch Centrum (AMC)
Emma Kinderziekenhuis/afd. H8
Meibergdreef 9, telefoon 020 - 5669111
Mevrouw Dr. M. Peters, Dr. H. Heyboer

Onze Lieve Vrouwe Gasthuis
1e Oosterparkstraat 279
telefoon 020 - 5999111
Polikliniek haematologie
Dr. K.J. Roozendaal, haemataoloog/oncoloog

Den Haag Leijenburg Ziekenhuis, Leyweg 275
telefoon 070 - 3592000
afdeling haematologie
Dr. P.W. Wijermans

Leiden Academische Ziekenhuis Leiden
Rijnsburgerweg 10, telefoon 071 - 5262267
afdeling haematologie
Prof.dr. A. Brand – transfusie therapie
Prof.dr. J.M.J.J. Vossen - beenmergtransplantatie

Rotterdam Sophia Kinderziekenhuis
Dr. Molenwaterplein 60
telefoon 010 - 4636363
Afdeling Oncologie/haematologie
Dr. I.M. Appel

Utrecht AZU/Wilhelmina Kinderziekenhuis
Nieuwegracht 137
telefoon 030 - 2504000
Afdeling haematologie
Mevrouw dr. H.M. van der Berg

Clinical genetics centers

Of heeft u vragen over onderzoek naar een erfelijke aandoening, dan kunt u daarvoor terecht bij een Klinisch Genetisch Centrum. Deze centra zijn verbonden aan de Academische Ziekenhuizen. Informatie over adressen en telefoonnummers vindt u op de site van de Vereniging Klinische Genetica Nederland: www.nav-vkgn.nl.

Beschikt u niet over internet, bel dan met de Erfolijn. N.B. Voor een bezoek aan een Klinisch Genetisch Centrum heeft u een verwijzing van de huisarts nodig.

Most central laboratories can diagnose Sickle Cell Disease and Thalassemia Major in the affected children and establish the carrier state for both diseases in the healthy parents seeking prevention.

The Hemoglobinopathies Laboratory and the DNA Laboratory of the Leiden University Medical Center are the reference laboratory for carrier diagnostics (Dr. P.C. Giordano) and prenatal diagnosis (Prof. B. Bakker)

Hemoglobinopathieën Laboratorium
Wassenaarseweg 72, 2333 AL Leiden
Telefoon 071 - 5276000
Zie ook www.hpbinform.com

Patientorganisation

OSCAR: organisatie Sikkel Cell Anemie **RELIEF**
(Stichting Sikkelcel Anemie en Thalassemie Nederland)
Van Nijenrodeweg 315
1082 HB Amsterdam
Telefoon 020 – 6797887 (van 20.00 – 22.00 uur)
Email: oscarsikkelcel@hotmail.com
www.erfocentrum.nl/oscar



Colofon

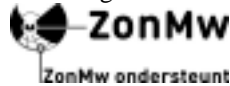
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Deze uitgave werd mede mogelijk gemaakt door:



Voor een overzicht van alle informatiematerialen kunt u contact opnemen met het Erfocentrum.

Vragen over erfelijkheid en gezondheid?

Bel, mail of surf

Erfolijn: 0900-66 555 66 (€0,10 per minuut)

Email: erfolijn@erfocentrum.nl

Website: www.erfelijkheid.nl

www.kalitim.nl

Het Erfocentrum is een initiatief van de Vereniging Samenwerkende Ouder- en Patiëntenorganisaties betrokken bij erfelijke en/of aangeboren aandoeningen (VSOP)