HEREDITARY HEMOLYTIC ANEMIA I

| SICKLE CELL DISEASE |

BASIC GUIDELINES
for patients and family

HEMORIO
BLOOD CENTER OF RIO DE JANEIRO

PATIENT'S MANUAL - HEREDITARY HEMOLYTIC ANEMIA (SICKLE CELL DISEASE) REVISED EDITION 05/2010

Introduction

The objective of this manual is to provide information about Sickle Cell Disease to patients and their relatives, as we know that medical information and its technical jargon can be difficult or incomprehensible to most people. Thus, we hope it can answer your questions.

Any comments are welcome, either about the clarity or omission of some information considered important they can be sent as suggestions to HEMORIO or by e-mail ouvidoria@hemorio.rj.gov.br.

What is Sickle Cell Disease?

Sickle Cell Disease is an inherited disease in which red blood cells in certain conditions modify their shape and become like a sickle, hence the name *sickle*.

It is necessary to know the characteristics of red blood cells (RBCs) in order to better understand the Sickle cell disease.

Function: The red blood cell operates carrying oxygen to tissues, constituting thus the main fuel for organs.

Composition: The red blood cells contain hemoglobin which is a protein rich in iron. The oxygen is picked up by hemoglobin, when it passes through the lungs. Oxygen is carried by red blood cells and distributed to various organs and tissues in the body. When the amount of hemoglobin is low, anemia occurs.

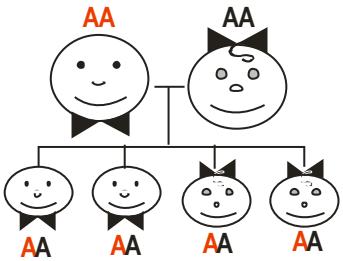
Evolution: The development of blood cells is a process called Hematopoiesis. Red blood cells enter the bloodstream after having already gone through the process of growth that occurs in bone marrow. Bone marrow is a soft tissue, like a sponge and it is found in the cavities of many bones. Adult red blood cells must be in adequate number to develop their functions properly. The red cell membrane should be extremely tough yet highly flexible and deformable to withstand the aggressions in circulation and move through tiny capillaries and "pores" of the spleen.

By losing their ability to function properly, they are destroyed by spleen and replaced with newer erythrocytes that go through the same process, and so on.In the case of sickle cell disease, red blood cells are destroyed (hemolysis), because of its sickle-shaped. They aggregate and cause blocked blood flow in small vessels of the body. With poor circulation in the affected organs, damage may occur, causing pain, destruction of blood cells, jaundice (yellow eyes) and anemia.

How do people get Sickle Cell Disease?

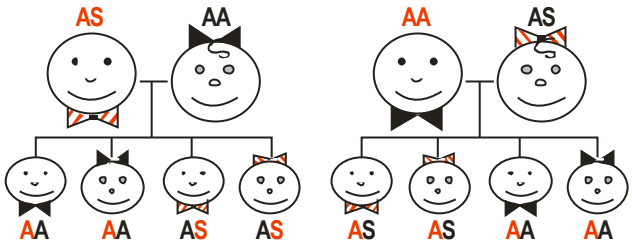
Hemoglobin, the pigment that gives color to red blood cells, is essential for the health of every organ in the body. It works carrying oxygen through the body.

The normal hemoglobin is also referred Hb A, and normal people are called AA, because each portion is inherited from both parents.

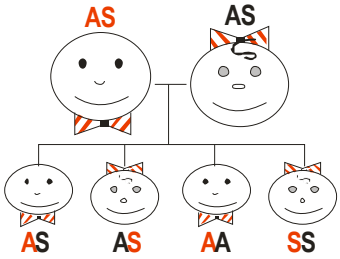


In sickle cell disease, the hemoglobin produced is abnormal and is called S. When a person receives hemoglobin A from a parent, and hemoglobin S from the other one, it is called "sickle cell trait," and it is referred as AS. People with sickle cell trait are not sick. They are usually asymptomatic and discovered to have this condition only when a family study is performed.

For example, if one parent has sickle cell trait (AS), there is a 50% chance with each pregnancy of having a baby with sickle trait (AS).



But if both parents have sickle cell trait (AS), there is 50% chance with each pregnancy of having a baby with sickle cell trait (AS) and 25% chance of having a baby with sickle cell disease (SS). Different from sickle cell trait, sickle cell disease can cause pain and lead to serious health problems.



What is the difference between Sickle Cell Disease and Sickle Cell Anemia?

Sickle Cell Disease is the name of a group of illnesses which hemoglobin S is present. There are many types of sickle cell disease, and Sickle Cell Anemia is one of the most common types, also called hemoglobin SS disease.

Hemoglobin S may be associated with other abnormal hemoglobin (C, D, thalassemia). In these cases, they are named hemoglobin CS disease, hemoglobin DS disease or hemoglobin S-thalassemia disease.

What are the signs and symptoms of Sickle Cell Disease?

Sickle Cell Disease (including SS, SC, SD, S-thalassemia) can manifest itself differently in each individual. Some have only a few mild symptoms while others have one or more signs or symptoms that we will describe:

1 – PAINFUL CRISES

Pain is the most common symptom of sickle cell disease, caused by obstruction of small vessels by sickle red blood cells. It may be located in the bones or joints, chest, abdomen, and can reach the whole body.

These crises have variable duration and can occur several times a year. They are usually associated with cold weather, infections, premenstrual, emotional problems, pregnancy or dehydration.

2 - JAUNDICE (YELLOW EYES)

It is the most common sign of the disease. When red cell is destroyed a yellow pigment called bilirubin appears in the blood. The urine becomes the color of Coca-Cola and

the whites of the eyes become yellow. It is not contagious and should not be confused with hepatitis.

3 - DACTYLITIS

In young children the pain crises may occur in the small vessels of the hands and feet, causing swelling, pain and redness at the site.

4- INFECTIONS

Infections may occur frequently located in the throat, lungs and bones. These infections should be evaluated by a doctor as soon as appear. All patients must be current on vaccinations as well as seek medical attention in an emergency room at the first sign of fever.

5 – LEG ULCERS

Due to the sickling of blood cells in small leg veins, poor circulation can occur, and consequently, open sores (ulcers) which are difficult to heal. This often occurs near the ankles.

The ulcers can take years to complete healing, if not properly cared for early. It is highly recommend the use of thick socks and shoes, and tetanus vaccine.

6 – ACUTE CHEST SYNDROME

It is a frequent complication in patients with sickle cell disease and its symptoms are shortness of breath and chest pain, with or without fever. Acute chest syndrome is very serious, and if it is suspected you should be urgently treated in hospital.

7 - SPLENIC SEQUESTRATION

It is a complication that usually occurs in children, caused by obstruction of the vessels of the spleen (an organ located at the top left side in the abdomen). This complication is an emergency and can lead to severe anemia. It needs urgent treatment with a blood transfusion. Your doctor should explain how to palpate your spleen, for you to control its size.

Living with Sickle Cell Disease

People with sickle cell disease should avoid heavy exercise, be fed with vegetables, fruit and meat, and drink plenty of fluids. It is important to wrap up during the cold and wear light clothing during the summer. The use of shoes and socks to prevent leg injuries are also recommended as well as regular medical checkups and treatment.

Can children attend school normally?

Children with sickle cell disease often face a school career in which their disease process hinders their ability to concentrate and may interfere with learning. Additionally you may need an increase in school programs, to retrieve possible failures during hospitalizations. Teachers should be counseled about the clinical and complications of sickle cell disease. Give a Manual on sickle cell disease to their teachers.

Can a sickle cell disease patient travel by plane?

Yes. High altitudes can lead to sickling crises; however, if you need to fly, there is no need to worry because all the major airlines have planes with pressurized cabins.

Can patients go to the beach on sunny days?

Yes, they can go to the beach before 10:00 am and after 3:00 pm, but should drink plenty of liquids. However, they should avoid diving, especially in cold water.

Can I play sport with sickle cell disease?

Yes, but exercise should be moderate. Excessive exercise can lead to painful crisis. Just make sure you hydrate a lot. You can also consult our physiotherapists for more information.

Can women with sickle cell disease have babies?

Yes, however, a pregnant woman with SCD is at a higher risk of having problems during pregnancy that can affect her health such as increased blood pressure, kidney problems, aseptic necrosis of the femur or humerus and greater need for transfusion. During pregnancy, sickle cell disease can become more severe and pain crisis can occur more frequently. Each case should be discussed with the doctor.

Can women with sickle cell disease use contraceptive?

Yes, but she should be accompanied by a medical specialist. Injectable contraceptive is an excellent contraceptive method for sickle cell patients and may even reduce the sickling crisis, reducing the incidence of pelvic inflammatory disease and the failure rate is less than 1%. Depot medroxyprogesterone acetate (DMPA) is the best studied form of birth control for women with sickle cell disease.

What is avascular necrosis of femoral head?

Some patients have obstruction of the small veins of the hip joint. In this case the head of the femur (thigh bone), with no blood circulation, suffers wear and shortens the leg.

In most cases, treatment should be started using crutches to relieve the burden on the affected limb. In some cases, surgery may be indicated. Patients should be accompanied by an orthopedic surgeon, physiatrist and hematologist.

What is priapism?

Priapism is unwanted, prolonged and painful erection of the penis, caused by obstruction of the vessels. It usually it occurs spontaneously at night.

When it occurs, you need to go to an emergency room immediately. Early treatment can prevent future complications.

Priapism can also occur in shorter and repeated episodes. Be sure to inform your doctor as it may prescribe medications to relieve symptoms.

Does sickle cell disease affect the kidney?

Yes, vessel blockage also occurs in the kidney and may lead to a series of changes in kidney function. Some patients can develop chronic renal failure.

How can it be identified?

You must regularly attend examinations and routine consultations with your doctor. If necessary, doctor will refer to the nephrologists.

Does sickle cell disease affect the brain?

Yes. It affects from 6% to 8% of patients with sickle cell anemia, especially between 2 and 10 years of age. They may have several neurological signs such as headache, seizures, dizziness and stroke.

This complication involves large vessels in the cerebral circulation. When the symptoms above occur, the patient should be referred to the emergency room or physician assistant who will ask for the evaluation of the neurologist.

Patients who are in neurological monitoring should be advised not to miss the regular visits or the use of prescribed drugs.

HEMORIO has a very modern device, the Transcranial Doppler, which is the only widely tested and validated method for stroke prevention in sickle cell disease patients.

Is there a cure for sickle cell disease?

Although there is no cure since it is hereditary, sickle cell disease can be controlled. Therefore it is necessary early diagnosis and frequent consultations attendance.

How is sickle cell disease treated?

The bases of the treatment of sickle cell disease are:
1 - Proper hydration
2 - Use of Folic Acid
3 - Use of Hydroxyurea
4 - Replacement blood
5 - Use of Penicillin
6 - Use of analgesics

Why are fluids used in sickle-cell crisis treatment?

Fluids are given either by mouth or through a vein, and help prevent dehydration; decreasing viscosity and they also improve blood circulation.

At home, you should drink an adequate amount of fluids with the same goal. Ask your doctor what is the most appropriate for you, considering your age, weight, height and other characteristics.

Why should I take folic acid?

Because the body produces many red blood cells tin order to compensate the anemia, and folic acid is an important vitamin in the formation of these globules. However, under normal conditions, a diet rich in vegetables, beans, egg yolk and milk is enough to restore the body's folic acid, and drug supplement is not essential.

And about Hydroxyurea?

Hydroxyurea is a drug used to treat various hematological diseases such as polycythemia vera and for some types of leukemia.

In Sickle Cell Disease, it works by increasing the amount of fetal hemoglobin in red blood cells. Fetal hemoglobin blocks the effect of hemoglobin S, improving anemia, reducing painful

crises, episodes of acute chest syndrome, frequency of hospitalization and need for transfusion.

What are the side effects and contraindications of Hydroxyurea?

This drug should be discontinued during pregnancy. In addition, women of childbearing age should use contraceptives and sign an informed consent, showing that they are aware of the prohibition to become pregnant, while taking the medication.

Hydroxyurea may cause bone marrow depression (low production of blood cells), and liver damage. These effects, however, were not observed in patients with sickle cell disease who used this drug for a long time.

There is a discussion about hydroxyurea treatment and predisposition to cancer in patients treated long term. In the United States, this drug is already being used since 1994 and so far there is no evidence that this bias occurs.

In which situations are blood transfusions indicated?

In the past, painful crises were treated with blood transfusion. THIS IS NO LONGER INDICATED.

Transfusion is indicated to treat worsening anemia and sickle cell disease complications, such as priapism, acute chest syndrome and splenic sequestration. It is indicated also in some cases, to prevent stroke.

What are the risks of blood transfusions?

Transfusion should be done with blood subjected to special techniques of classification (phenotyping) as well as filtration, which reduces the risk of many of transfusion reactions. However, despite all tests, there is a residual risk of transfusion-transmitted infection, such as hepatitis and HIV.

What is phenotyping?

Phenotyping is a kind of blood test that ranks not only for ABO and Rh type, but also for many other blood systems.

It is a more complete classification, which aims to provide more security for blood transfusion. This type of procedure has been done at HEMORIO since 1998.

What is blood transfusion filtration?

It is a technique in which the blood passes through a "filter" that retains some special elements of the blood, such as leukocytes, which can cause febrile reaction. This procedure is performed at HEMORIO whenever indicated.

What about the use of sodium bicarbonate?

Although there is acidosis in the sickling process, sodium bicarbonate, either oral or intravenous, does not reach the interior of the red blood cell. Thus, this procedure, which was common in the past, is no longer indicated.

Why is penicillin used?

Prophylactic antibiotic (prevention of infections), is always indicated for sickle cell disease patients until the age of 5. This practice is recognized as a major advance in treating this disease, avoiding serious complications.

It should be noted that the daily use of antibiotics, does not "spoil the teeth" does not "cause diarrhea, stomach pain or vomiting and does not decrease the appetite as well". If there is any doubt, talk to your doctor about it.

What about the use of analgesics?

Pain should be seen as a symptom, which although frequent, is not normal. The deal will be effective if the management follow these rules:

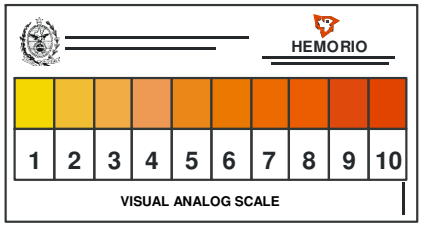
1 - When the pain occurs, it is necessary to maintain the use of analgesics, for a minimum of 24 hours after the relief of pain;

2 - A single dose of an analgesic is generally not enough for the rapid relief of pain;

3 -The use of analgesics should be continuous;

4 - For each level of pain, treatment must begin differently;

5 - The level of pain should be measured by a Visual Analog Pain Scale (see illustration).



How to Use a Visual Analog Pain Scale

The chart below summarizes the steps to be followed, according to the degree of pain. Your doctor will provide appropriate guidelines.

PAIN INTENSITY	START OF TREATMENT	AFTER 24 H WITHOUT PAIN	AFTER MORE THAN 24 H WITHOUT PAIN	RECURRENCE OF PAIN
1 2 3	DIPYRONE PO 8/8H STOP AFTER 24H WITHOUT PAIN	REMOVE DIPYRONE		
4 5 6	DIPYRONE PO 8/8H INTERIM DICLOFENAC PO 8/8 H - UNTIL 24H WITHOUT PAIN	REMOVE DICLOFENAC AND KEEP DIPYRONE PO 6/6 H FOR 24 H		GO TO EMERGENCY ROOM
7 8 9 10	DIPYRONE PO 8/8H INTERIM DICLOFENAC PO 8/8 H INTERIM CODEINE PO 4/4 H UNTIL 24H WITHOUT PAIN	REMOVE DIPYRONE AND KEEP CODEÍNE PO 8/8 H INTERIM DICLOFENAC PO 8/8 H	REMOVE CODEINE AND KEEP DICLOFENAC FOR 24 H	

Why patient should not take medicines that contain iron?

Because the red blood cell is destroyed releasing iron into the circulation. This iron is stored in tissues, which may lead to the development of chronic injuries. If the patient receives many transfusions or takes iron-containing compounds over years, the iron deposited in the body can eventually cause the patient to have heart dysfunctions, liver problems or diseases like diabetes.

What can I expect from HEMORIO for my treatment?

There are many factors that influence the evolution of patients with Sickle Cell Disease. Thus, we believe that the most appropriate care should be done by professionals specialized in different areas of interest to follow these individuals.

HEMORIO is pioneer in this type of approach, with the effective work of a comprehensive group, since 1996, composed by physicians (hematologist, pediatrician, hemotherapist, and gynecologist), dentist, nurse, social worker, nutritionist, physiotherapist and psychologist.

What is the role of the physiotherapist in the treatment of sickle cell disease?

The physiotherapist must evaluate patients and plan individual physical therapy in accordance with their motor, respiratory, neurological and postural conditions.

During hospitalization, the therapist should monitor patients who need physical therapy or suffer from respiratory failure, and guide the attitudes that must be taken in bed, avoiding deformities or inappropriate movements of patients, especially children with neurological problems.

In some situations, physical therapy can prevent certain deformities, such as equinus foot that may occur in some cases of leg ulcers.

And finally, respiratory physiotherapy is considered an excellent tool to prevent acute chest syndrome. All patients should receive respiratory therapy to prevent thoracic events.

How should sickle cell disease patients eat?

Since there is a state of higher caloric needs of the body caused by anemia, the diet must be balanced. Bread, margarine, milk and dairy products, sugar, cereals, beans, lentils, peas, and chick peas must be present in daily meals, as well as meat (beef, chicken or fish) vegetables, fruit, and vegetable oil (3 tbsp divided into 3 meals).

As sickle cell patients have high inventory of iron in the body, iron-rich foods such as the following ones, although not prohibited, must be avoided or consumed with moderation: offal (liver, tongue, heart and kidneys), marine animals with shells, nuts, eggs, molasses, wheat breads whole and enriched grains and fortified food.

It is important to drink plenty of fluids. Tea reduces iron absorption and therefore, should be taken in abundance during meals, since the supply of iron is increased in sickle cell disease. Between meals, foods rich in vitamin C as orange, lemon, tangerine, cashew, pineapple, guava, mango, melon, strawberry, are all recommended, as well as leafy vegetables such as beets, cabbage, raw lettuce, peppers, and tomatoes. Specific diets should be deployed in case of complications.

What is the role of Social Work in Interdisciplinary Team?

Social work has as specific activities:

To evaluate the socioeconomic, housing and professional conditions of the patient's family

To provide information about HEMORIO.

To inform patients of Social Security rights.

To provide patients and their families with information on resources and community services.

To follow admitted patients in order to reduce the negative effects of hospitalization.

To encourage experience exchanges between patients and their families.

To provide educational information on sickle cell disease.

To provide condoms.

How can the psychologist help me?

There is a close connection between body and mind. Living with Sickle Cell Disease can influence on the patients' psychological state, which can affect their body. The counseling is intended to help clarify the difficulties arising from this interrelationship.

The family can also receive counseling, to assist in understanding the child's behavior as well as children in living with her parents.

How can patients take care of their teeth?

The work of dental service has the following purpose:

- Teach parents and children cause and effect relationship between sugar and tooth decay.

- Find the habit of not eating between meals. When it is not possible, opt for non-sugary foods like fruit and milk. If brushing is not possible, make at least mouthwash to clean teeth.

- Perform a high frequency of tooth brushing always after the main meals and at bedtime.

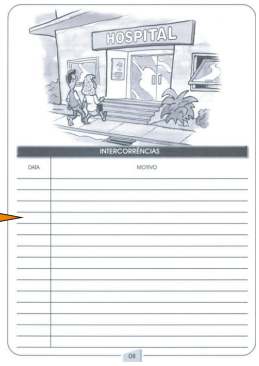
- Floss daily.

- Go to the dentist regularly for early diagnosis of caries. The dentist will apply fluoride to teeth from two years of age on, every three months.

How should I use the Handbook and Guidance Notes of the Patient?

The Patient Handbook is a kind of "diary" on which you should write down your daily complications, bringing it to each outpatient visit, to show your doctor.

Place for your notes



What if the patient is in pain crisis and cannot come to HEMORIO?

The patient must go to an emergency room and show his Patient Handbook to the doctor.

Is there any patient association?

AFARJ, Association of sickle cell and thalassemia Rio de Janeiro, based at HEMORIO – 8, Frei Caneca Street, room 801, Rio de Janeiro - RJ- ZIP CODE: 20.211-030 phone: 2332-8611, ext 2246.

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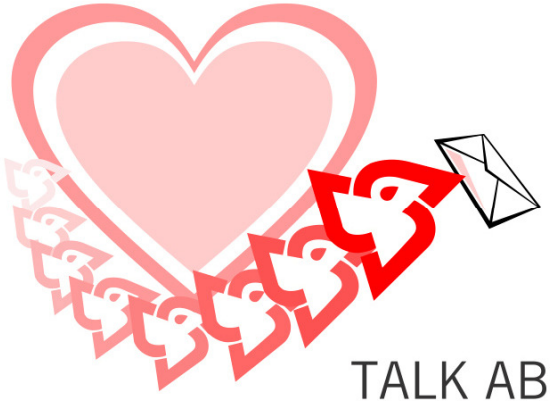
GO TAKE A
MESSAGE OF LOVE.



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