Sickle Cell Disease

A booklet for parents, patients and the community

By Adlette Inati-Khoriaty MD

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'UNITY IS OUR STRENGTH'

'MOVING FORWARD TOGETHER FOR BETTER HEALTH AND QUALITY OF LIFE FOR PATIENTS WITH HAEMOGLOBIN DISORDERS'

THALASSAEMIA INTERNATIONAL FEDERATION

'MOVING FORWARD TOGETHER TOWARDS IMPLEMENTATION OF THE WHO RESOLUTIONS':

1. **RESOLUTION WHA59.20 - 27 May 2006** on Sickle-cell anaemia, AND;
2. **RESOLUTION EB118.21 - 29 May 2006** on Thalassaemia and other haemoglobinopathies

About the Author

Dr Adlette Inati-Khoriaty received her medical degree from the American University of Beirut and completed her Paediatric Residency and Paediatric Hematology-Oncology Fellowship at Children's Hospital Medical Center and Sidney Farber Cancer Institute - Harvard Medical School- Boston. She is American Board certified and is a member of the Alpha Omega Alpha Honor Medical Society.

Dr Inati has contributed significantly to clinical scientific research and patient care and has been recognized for her unwavering commitment to the control of inherited haemoglobin disorders worldwide. She has published extensively and has been a reviewer and a guest editor for reputable medical journals.

***Dr Inati runs the largest sickle cell disease clinic in Lebanon** and has initiated the first Middle East Thought Leaders and Investigators Sickle Cell Disease Scientific Meeting as well as sickle cell disease prevention and early detection campaigns in Lebanon and the region*. Currently, she is the Head of the Paediatric Haematology Oncology Division and the Medical Director of the Children's Center for Cancer and Blood Diseases at Rafik Hariri University Hospital and is a consultant haematologist at the Chronic Care Center, Beirut, Lebanon.

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Dr Eleftheriou obtained her graduate and postgraduate degrees (BSc Hons,MSc, PhD) from the University of London, the Centre for Disease Control, Atlanta, USA and the University of Leicester in Biochemistry, Microbiology, Virology and Business Administration. She served for many years as Director of the Virus Reference Centre of the Cyprus Ministry of Health and the WHO Cyprus Collaborating Centre, and *recently as Executive Director of Thalassaemia International Federation*. In the above capacities, and through serving as a WHO consultant and as author of many publications, *she has worked with patients, health professionals in the field and policymakers to serve the cause of haemoglobin disorders for over three decades.*

Michael Angastiniotis - MD

Graduated in Medicine from the University of Aberdeen Scotland in 1966. *He is the Ex-Director of the Paediatric Department of Archbishop Makarios III Hospital as well as the Thalassaemia Centre, and a Past President of the Cyprus Paediatric Association. Currently, he is the Medical Advisor for the Thalassaemia International Federation.* He has had an active involvement with the World Health Organisation as a member of the Committee for the Control of hereditary Anaemias, a member of the WHO Expert Advisory Panel on Human Genetics and has had the role of Special Advisor and Short Term Consultant for the Control of Haemoglobinopathies in the Eastern Mediterranean region.

Preface

The aim of this booklet *is to provide families of patients affected with sickle cell disease (SCD) with accurate and concise information about SCD, in order to help them obtain the best possible treatment for their children.* The booklet also aims to give parents information that will contribute towards diagnosis at an early and reversible stage, allowing them to seek timely help and prevent often devastating complications. It will also help parents to cope with the disease and enable them to play an active role in the care of their children under medical supervision, promoting ways of dealing with their children in a positive, supportive and disciplined manner.

In addition, the booklet can be used by health professionals to educate parents and patients about SCD, and schools may find it useful in educating teachers and students about this highly prevalent disease.

The information available in this booklet is up-to-date, scientific, reliable and phrased in a simple and clear manner which can be easily understood by families and older patients. We hope that parents and older patients will find this booklet a helpful reference about the disease and ways of preventing complications. The more parents and older patients know, the more people with SCD can be salvaged, allowing them to lead a happy and productive life, with a survival almost comparable to healthy individuals.

The information given in this booklet represents the opinion of the author, and is the product of long experience in handling patients with SCD and dealing with the multi-faceted health problems faced by these patients and their families. The facts quoted here **are derived from landmark scientific studies that have been conducted on a large number of patients, and are based on solid evidence.** Other health providers may have opinions and practices which may differ in some ways from those cited in this booklet.

We would really welcome feedback from parents, patients and health providers, and would aim to incorporate this in future booklets. If you provide feedback, we will be working together for a better and a healthier future for children, adolescents and adults with sickle cell disease.

Adlette Inati-Khoriaty

Contents

Foreword by the President of Thalassaemia International Federation

Advances in the prevention, diagnosis and treatment of haemoglobin disorders, especially thalassaemia and sickle cell disease (SCD), have had a huge impact, both on the incidence of these disorders and patients' health.

With the development of new treatment protocols, patients fortunate enough to be able to afford and access state-of-the-art treatment can expect to live longer, and to have more productive lives. Convinced that indeed ***"Unity is our Strength"***, the Thalassaemia International Federation (TIF), with its ever-expanding and constantly developing educational programme, is committed to improving the health and the quality of life of every patient with thalassaemia, wherever he/she may live, irrespective of nationality, region or social status.

Our work to help control thalassaemia across the world received an important boost in the form of *WHO Resolution WHA59.20 (27 May 2006) on sickle cell anaemia and WHO Resolution EB118.R1 (29 May 2006) on thalassaemia and other haemoglobinopathies.* TIF is using these resolutions as a platform for promoting policies for their effective control, embracing the needs of all patients with Hb disorders and their parents for better health, better quality of life, and a better future, irrespective of a patient's specific disease, nationality, language, religion or culture.

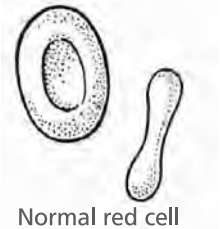
TIF often visits countries that are affected not only by thalassaemia, but also by SCD, and over time has confirmed the importance of providing basic information in an accessible form to those that need it. This booklet aims to meet that need, drawing on the specialist knowledge and experience of a medical expert in this field. The booklet contains important information about SCD and its management, presented in a simple and patient/parent-friendly manner. Whether you are a carrier or a patient or a parent, or simply interested in finding out more about SCD, this booklet offers a good overview of the main issues.

TIF is greatly indebted to the author, ***Dr Adlette Inati-Khoriaty.*** *We would also like to thank* ***Dr Androulla Eleftheriou*** *(TIF Executive Director) and* ***Dr Michael Angastiniotis*** *(TIF Medical Advisor) for their advice and input.*

Panos Englezos
President
Thalassaemia International Federation

Introduction

Sickle cell disease is an inherited disorder of the red blood cells. Red blood cells carry oxygen to all parts of the body through a protein called haemoglobin. ***Haemoglobin*** *is the red, iron-rich protein that gives blood its red colour and carries oxygen from the lungs to all parts of the body, and carbon dioxide waste from other parts of the body to the lungs so that it can be exhaled.* Normal red blood cells contain only normal haemoglobin and are shaped like doughnuts. These cells are smooth, flexible and move easily through small blood vessels to perform their vital function. *But in sickle cell disease, the red blood cells contain an abnormal haemoglobin called* ***sickle haemoglobin***, which causes these cells to change to a stiff, sticky, curved shape like sickles or crescent moons. It is this sickle shape of the red blood cells that gives "sickle cell" disease its name. Sickle cells die prematurely, resulting in anaemia. They also pile up, become stuck and form plugs in small blood vessels, thus slowing or blocking blood flow and oxygen to certain parts of the body. This produces pain, results in tissue damage and can lead to the serious complications of sickle cell anaemia.



Normal red cell

Sickle cell

What causes sickle cell disease

"An inherited disease is one which is passed from parents to their children through genes."

All forms of sickle cell disease are inherited and can never be acquired with time. *An inherited disease is one which is passed from parents to their children through genes.* Genes are substances within the father's sperm and the mother's egg that determine all characteristics in a baby. *Children inherit pairs of genes from their parents for almost every physical characteristic they have, including their haemoglobin type.* Each of our parents has two genes for haemoglobin, located on chromosome 11, but they pass only one of these genes on to each child. Which gene is passed on is a matter of mere chance. Sickle cell disease is caused by a mistake in the gene that tells the body to make haemoglobin. Consequently, sickle haemoglobin is formed. The sickle gene is particularly common among people with African, Mediterranean, Latin American and Indian ancestry. In the United States, it most commonly affects African-Americans and Hispanics.

To inherit sickle cell disease, a child must get the sickle (S) gene from one parent and a sickle (S), C, or B (beta-thal) gene from the other, which means that both parents are carriers or have the trait. If both genes passed on from parents are for the usual haemoglobin A, the child will have normal haemoglobin and will not have sickle cell disease. If both genes are passed on for sickle haemoglobin, the child will have sickle cell anaemia – the commonest form of sickle cell disease – and his/her body can make only sickle haemoglobin. Persons who inherit one gene for normal haemoglobin and one gene for sickle haemoglobin will have sickle cell trait, and are called carriers. Their bodies make both normal haemoglobin and sickle cell haemoglobin. Sickle cell trait or carrier state is not a disease, and does not change to a disease. But a person who is a carrier can pass this trait on to her/his children, exactly as his/her parents passed the trait on to her/him.

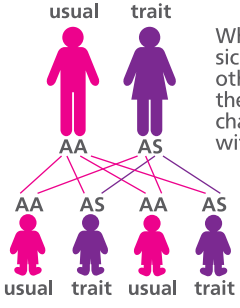
When both parents have sickle cell trait, for each pregnancy, the chances are:

- 1 in 4 that the baby will have only normal haemoglobin
- 2 in 4 that the baby will have both normal and sickle haemoglobin (sickle cell trait)
- 1 in 4 that the baby will have only sickle haemoglobin (sickle cell anaemia)

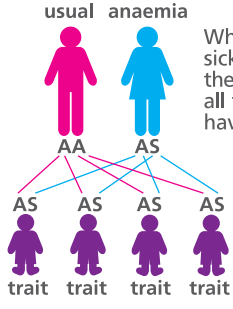
The chances are the same for each pregnancy with the same partner.

Inheritance scenarios

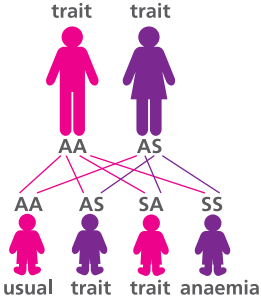
The sickle cell gene is passed from generation to generation in a pattern of inheritance called autosomal recessive inheritance. You can find below various inheritance scenarios seen in real life. ***"Usual"*** *indicates a person with two normal haemoglobin genes (AA).* ***"Trait"*** *means a carrier, in other words a person who has one normal haemoglobin gene and one sickle gene (AS), while* ***"anaemia"*** *indicates a person who has two sickle genes (SS) and cannot make any normal haemoglobin, and thus has the disease state.*



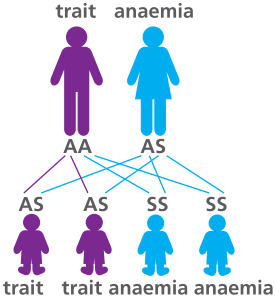
When one parent has sickle cell trait and the other is a non-carrier, they have a 50% (1 in 2) chance of having a baby with sickle cell trait



When one parent has sickle cell anemia and the other is not a carrier, all their children will have sickle cell trait



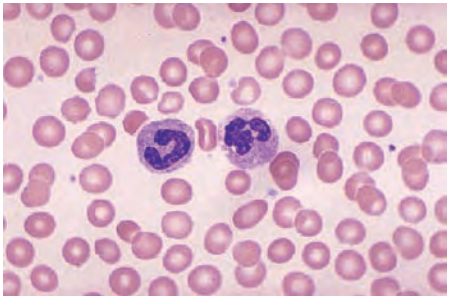
When both parents have sickle cell trait, they have a 25% (1 in 4) chance of having a baby with sickle cell disease



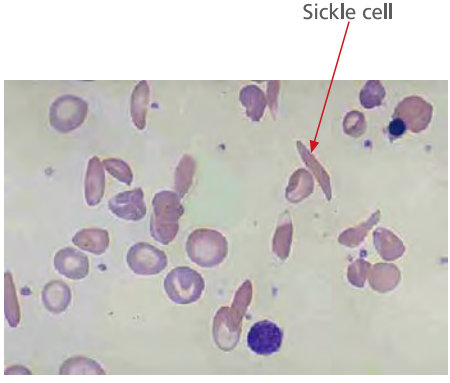
When one parent has sickle cell anemia and the other has sickle cell trait, 50% of their children will have sickle cell anemia and 50% sickle cell trait

Diagnosis of sickle cell disease

Doctors diagnose sickle cell disease through ***one of two blood tests*** which check for the defective form of haemoglobin. *The first is called* ***haemoglobin electrophoresis****, and this is the most widely used test. The second is a newer test called* ***high performance liquid chromatography (HPLC)****. A third test, which is simple and readily available, is the blood smear.* A sample of blood is examined under a microscope to check for the presence of sickled red blood cells. These three diagnostic tests are available in most labs, and are rapid, sensitive and relatively inexpensive.



Normal blood smear



Sickle cell disease smear

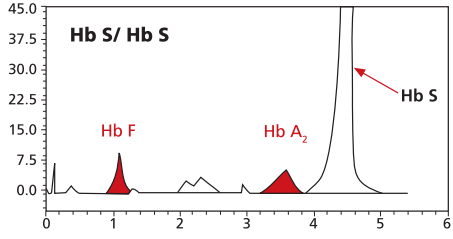
Types of sickle cell disease

The three commonest types of sickle cell disease are: ***haemoglobin SS*** *(**Hb SS** or **sickle cell anaemia**),* ***haemoglobin SC*** *(**Hb SC**)* ***disease*** *and* ***haemoglobin sickle beta thalassaemia***. Each of these types can cause sickle pain episodes and complications, but some are more severe than others. The name "sickle cell anaemia" is commonly used interchangeably with "sickle cell disease", but they are not the same. ***Sickle cell anaemia*** *is the commonest and most severe type of sickle cell disease*, where the gene for sickle haemoglobin is inherited from both parents and results in the production of only abnormal sickle haemoglobin.

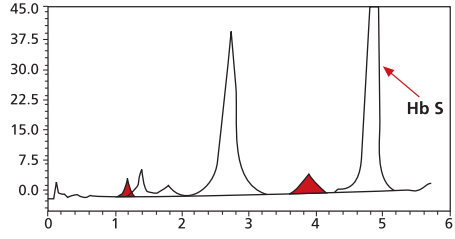
In ***haemoglobin SC disease***, one parent passes down the sickle gene, while the other parent contributes the C gene type of haemoglobin. This form is less severe than sickle cell anaemia.

Similarly, a child with ***haemoglobin sickle beta thalassaemia*** *(**Sβ thal**)* inherits one sickle gene and one beta thalassaemia gene, which produces either a decreased amount of haemoglobin or none at all. If no haemoglobin is produced, *the condition is called* ***Sβ^0 thal***, and the clinical picture is similar to sickle cell anaemia. If the amount of haemoglobin produced is decreased, *the condition is called* ***Sβ$^+$ thal*** *and this is less severe than sickle cell anaemia*. Sickle beta thalassaemia has a high prevalence in the Mediterranean area and has a clinical presentation which is similar to sickle cell anaemia and different from beta thalassaemia.

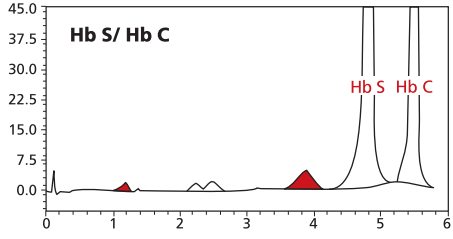
So sickle cell disease results not only from the inheritance of two sickle haemoglobin genes, but also from one sickle haemoglobin gene combined with another abnormal haemoglobin gene. *While there are certain differences amongst these various syndromes, their symptoms are often quite similar.*



HPLC of a patient with sickle cell anaemia (HbSS)



HPLC of a patient with sickle ß+ thalassaemia (Sß+ thal)



HPLC of a patient with sickle haemoglobin C (HbSC)

Do all people with sickle cell disease have the same clinical manifestations and outcome?

The signs and symptoms of sickle cell disease vary greatly from one person to another. Some affected people are quite healthy and are diagnosed at a relatively old age; others are frequently hospitalised and have many complications, while some die at an early age from the disease and its complications. The reasons for this marked variability in the clinical spectrum of this disease are not all known, and a serious effort is being made by sickle cell disease researchers to understand this phenomenon.

Sickle cell disease affects different people in different ways and no one can accurately predict the seriousness of the disease early on.

Nevertheless, certain patient and environment related factors do make a difference in the outlook of people with sickle cell disease:

a. The type of sickle cell disease.
b. How early the diagnosis is made and how soon the treatment is given
c. The kind of care a person gets.
d. How the person and the people around him, particularly parents, deal with the disease.

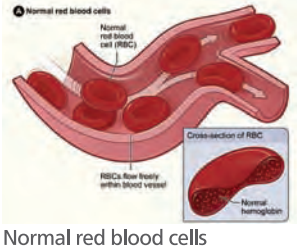
In general, sickle cell anaemia is more severe than sickle beta thalassaemia or sickle C disease. Children who are diagnosed at birth and receive penicillin prophylaxis and appropriate vaccines appear to fare much better than those diagnosed later. Patients who are treated in special sickle cell disease centres and by teams of specialists have better outlook than those treated in smaller and unspecialised centres. Most importantly, actively-involved ***parents with good knowledge about the disease and about ways of building up an independent and assertive personality for their children do play a major role in creating a better and a healthier life for their children.*** Adolescents and adults who receive good parental guidance early on, who comply with doctor's instructions and accept their disease fare much better than others who do not.

People with sickle cell anemia have perfectly intact minds with normal levels of intelligence. Some of them can be brilliant and are prime movers in their societies.

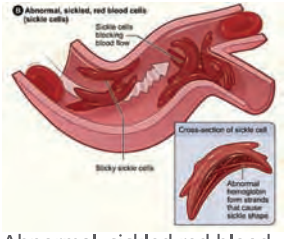
Most frequent medical problems in sickle cell disease

Pain

Periodic episodes of pain, called crises, are the hallmark and the most distinguishing feature of sickle cell disease. Pain develops when the sticky rigid sickle red blood cells get stuck in small blood vessels and block blood flow through these vessels in various vital body organs in the chest and abdomen, as well as in joints and bones. This process is called ***vaso-occlusion***, and is responsible for many of the health problems encountered in sickle cell disease. Consequently, no red blood cells and no oxygen can reach the tissues, and pain ensues because of lack of oxygen. *The pain mostly involves the bones, joints, abdomen and chest. It may vary in intensity and frequency between patients and also in the same patient, and can last for a few hours or a few weeks.* Some people experience only a few episodes of pain, while others experience crises on a monthly basis, necessitating hospitalisation and intravenous pain killers (analgesics). At certain times, pain can be extremely excruciating and incapacitating. In general, older patients get more frequent and more severe pain than younger patients. Dehydration (lack of fluid in the body), fever, temperature extremes, low oxygen and excessive fatigue are common triggers for pain.



Normal red blood cells



Abnormal, sickled red blood cells (sickle cells)

Anaemia

Healthy red blood cells have an average life span of about 120 days, after which they die and need to be replaced. However, sickle red blood cells are fragile and die prematurely after only 10 to 20 days, resulting in anaemia. People with sickle cell disease can also get worsening anaemia due to blood becoming entrapped in a suddenly-enlarging spleen ***(acute splenic sequestration)*** and/or a stop in the formation of new red blood cell ***(aplastic episode)*** due to certain infections and/or excessive red blood cells breakdown ***(hyper-hemolytic crisis)***. *Symptoms of anaemia include pallor (yellow skin colour), getting tired easily, irritability, loss of appetite and poor growth.*

Frequent infections

Infants and young children with sickle cell disease are extremely vulnerable to life-threatening infections in the ***lungs (pneumonia), blood (sepsis), lining of the brain (meningitis) and bone (osteomyelitis).*** Children under the age of five are at highest risk for these infections. The most worrisome infections are caused by a few types of bacteria, including

Streptococcus pneumoniae ***(pneumococcus)****, Haemophilus influenzae type b* ***(Hib)****, Neisseria meningitidis* ***(meningococcus)*** *and* ***Salmonella***. Other infections that children with sickle cell disease are vulnerable to are those caused by flu viruses. Because their immune systems – particularly their spleens – do not work normally, these children develop infections caused by the same germs that afflict other children, but they get these infections more frequently, become very ill faster, and are more likely to develop severe complications, or even die. Adolescents and adults can fight these infections much better than young children, because their immune system is stronger. Sickle cells can block the blood vessels of the spleen, like any other organ. With repetitive blockage, *the spleen undergoes infarction and subsequent damage, and usually stops functioning* ***(autosplenectomy)*** *in most affected people by the age of 5, except in the case of some Mediterranean patients*, where big spleens persist until a relatively old age. The spleen, which is located in the upper-left part of the abdomen, functions as part of the body's defence against infection by serving as a filter to remove bacteria from the bloodstream. A damaged spleen, like an absent spleen or absent lymph nodes, makes a child more vulnerable to serious and sometimes fatal infections. Infections are treatable and complete recovery is possible only if they are recognised and treated early enough. Fortunately, death from infections has declined dramatically since affected children began to be identified very early on in the newborn period, and started receiving prompt medical care to help prevent complications, including the antibiotic penicillin and necessary vaccines to protect them against some serious infections.

Be aware that:

- A child with sickle cell disease is at much higher risk of serious and potentially fatal infections than most other children.
- Any infection in a child with sickle cell disease is an emergency.

Body organ damage and failure

Sickle cells can block blood flow in blood vessels, thus depriving organs of blood and its nutrients and of oxygen. In sickle cell disease, blood is also chronically low on oxygen. Chronic deprivation of oxygen-rich blood due to repetitive plugging of the tiny blood vessels supplying these organs with sickle cells can result in tissue damage. All organs are vulnerable, including the kidneys, liver, spleen, heart and eyes.

If children are not treated optimally and early, as they grow older they will have poor function of their kidneys, liver, spleen, heart, eyes, etc., and ultimately will face organ failure and death. Fortunately, early detection of the disease and proper treatment will minimize this serious complication in the majority of patients. This is possible if patients are enrolled in a special sickle cell centre upon diagnosis and at a very young age, preferably the newborn period.

Other medical problems

Stroke

Stroke is one of the most catastrophic and frequent medical problems encountered in sickle cell disease. It is seen mostly in sickle cell anaemia and in young children. It can occur if sickle cells block blood flow to an area in the brain, resulting in decreased oxygen delivery and brain injury. Less frequently and more so in adults, stroke can be due to bleeding in the brain. A stroke can be overt with clear symptoms, or silent and detected only on special imaging studies such as MRI. *The best way to know if your child is at high risk for getting a stroke is by having him/her have a special test called* ***transcranial Doppler (TCD)***. This test can measure the velocity of blood flow to the brain. Researchers have recently shown that when this test is abnormal, a child is at high risk of getting stroke, and immediate preventive treatment must be given. Unfortunately, this test is available in only few centres in the world.

The signs and symptoms of a stroke include any of the following symptoms, alone or in combination: severe headache, fainting, seizure, sudden weakness or numbness of an arm or leg or the whole body, abnormal eye movement, asymmetric facial movement, change in the level of consciousness, and abnormal speech. You need to take your child to the hospital as soon as possible whenever any of these signs appears in your child. A stroke can be fatal and can often result in significant unfavourable conditions (sequalae).

Acute chest syndrome

This life-threatening complication is the second commonest cause of death in sickle cell disease patients after infection. It is more frequent in children than in adults, and in sickle cell anaemia compared to other sickle cell disease forms. Acute chest syndrome is characterised by chest pain, fever, cough, difficulty in breathing and an image on chest x-ray similar to pneumonia. The symptoms and signs of this condition are similar to those of a lung infection (pneumonia). Acute chest syndrome is caused by trapped sickle cells in the blood vessels of the lungs or by an infection. Recurrent attacks can damage the lungs. It requires immediate hospitalisation and medical treatment.

Acute splenic sequestration

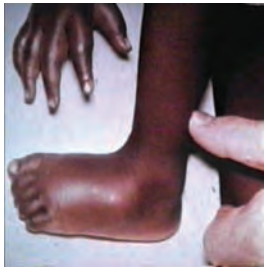
In most children with sickle cell disease, the spleen stays enlarged for several years, and in some cases can rapidly entrap red blood, resulting in ***the sudden onset of severe anaemia and in a state similar to internal bleeding. This condition is called acute splenic sequestration.*** Usually, by 6 years of age acute splenic sequestration is no more frequent, because the spleen of children with sickle cell anaemia usually becomes small due to scarring from recurrent sickling. However, in the Mediterranean area, where sickle cell anaemia is characterised by persistent big spleens beyond 6 years, and in children with SC disease and S-beta thal disease, it is common to see acute splenic sequestration at an older age, and sometimes in adulthood.

Acute splenic sequestration is a leading cause of death in children with sickle cell disease. It is a medical emergency and can be fatal in a few hours. The child becomes very pale and lethargic, and develops rapid breathing, a thumping (palpable) heartbeat and

bloating (abdominal distension) due to a huge spleen. If any of these signs and symptoms appears, you need to take your child to the emergency room immediately. It is important that you learn from your doctor about signs and symptoms of severe anaemia, as well as how to palpate your child's spleen.

If your child becomes very pale, lethargic and has abdominal distension, think of acute splenic sequestration and seek immediate medical attention. If you don't do this, **your child may die within hours.**

Hand-Foot syndrome



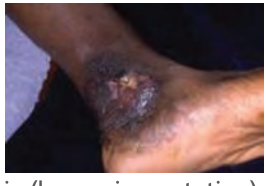
Swollen, painful, and sometimes red hands and feet (dactylitis or hand-foot syndrome) are often the first signs of sickle cell anaemia in babies. This is caused by sickle-shaped red blood cells blocking blood flow in small blood vessels in the bones of hands and feet. Dactylitis is a distinguishing sign of sickle cell disease, and when it appears in a child it should alert both parents and healthcare providers to the diagnosis of sickle cell disease. It is seen in about one-third of children with sickle cell disease under 3 years of age. Usually, it disappears in a few days without any lasting effects.

Gallstones

About a third of people with sickle cell disease have gallstones by the age of 18. *The breakdown of red blood cells produces a substance called **bilirubin**.* A high level of bilirubin can also lead to thick biliary sludge and gallstones, *and is responsible for a yellowing of the skin **(jaundice)** and eyes **(icterus)** in people with sickle cell disease.* Gallstones can result in severe abdominal pain, usually radiating to the shoulder.

In general, gallstones are not harmful. *But if they get stuck in the gallbladder duct, they can cause **a life-threatening infection of the gallbladder (cholecystitis)** with possible blood infection **(sepsis)**.* Eyes that are very yellow can be a sign that gallstones are stuck in the duct. Often, there is pain in the right side of the abdomen, which is a warning sign before the stones get stuck. If your child develops a fever, with increasing jaundice and very yellow eyes, together with right-sided upper abdominal pain radiating to the shoulder, be sure to call the doctor immediately.

Leg ulcers



These painful lesions are seen in 10 to 20% of sickle cell anaemia patients, and usually appear between 10 and 50 years of age. They are more common in males than in females, and are aggravated by hot climate, trauma, infection and severe anaemia. Typically, they are open elevated sores with surrounding skin redness and thinning, located within patches of skin that are darker than the normal surrounding skin (hyperpigmentation). They are mostly seen on ankles and can be single or multiple. Some heal rapidly, while others become chronic or recurrent. If present, seek medical attention promptly.

Avascular necrosis

This condition is seen when the blood flow to body areas with poor baseline blood supply is slowed and obstructed by sickle cells, ***leading to tissue breakdown (necrosis)***. It occurs mostly in the ***hip (femoral head)*** which suffers a l***oss of blood flow (avascularity)*** due to obstructive sickle cells. Other vulnerable joints are ***the shoulder (humeral head).***

Avascular necrosis usually occurs between the ages of 30 and 50, and is not seen frequently in children. When the hip-bone is involved, a painful limp is usual, and with walking, more pressure and damage ensue and the condition becomes chronic. Methods to prevent or minimise the risk of developing avascular necrosis include: gentle and controlled exercise of the shoulders and hips, avoiding jogging, doing leg-lifts in a sitting position and lifting light weights.

Kidney and bladder problems

Bladder and kidney infections are quite common in sickle cell disease. ***The symptoms of these infections are painful and frequent urination, the inability to control urine, low abdominal and back pain and fever.*** Another problem, which can last for hours or for days, is blood in the urine due to bleeding from the kidney. The longer it lasts, the more serious it is. Testing the urine will show if there is infection and/or bleeding.

Other problems include kidney damage by sickle cells, resulting in inability to concentrate urine, passing more urine and bedwetting to an older age. Because of this excessive water loss in urine, dehydration is more common in children with sickle cell disease than in other children. With repetitive clogging of the blood vessels which nourish the kidneys, renal failure can develop.

Priapism and Impotence

Men with sickle cell anaemia may experience painful, hard and sustained penile erections, a condition called priapism. This is seen at any age and is due to prevention of blood flow in the penis by sickle cells. It can last for a few minutes, but sometimes can last for hours. *Over time, priapism can damage the penis and lead to impotence in men with sickle cell anaemia.*

Stunted Growth

Red blood cells provide the body with the oxygen and nutrients needed for growth. ***A shortage of healthy red blood cells can slow growth in infants and children and delay puberty in adolescents.*** As they become adults, most children with sickle cell disease reach full size. If your child is smaller than his/her friends and or has delayed puberty, reassure him/her that he/she will most likely catch up in few years.

Eye Problems

Sickle cell disease can cause eye damage and, rarely, blindness. The back of the eye ***(retina)***, which is the most important eye part for vision, contains tiny blood vessels that can become clogged by sickle cells. This can cause bleeding or scarring at the back of the eye. Early eye checkups can detect this problem at a stage when it may be treated successfully.

Treatment

Sickle cell disease is a chronic disease which accompanies the child throughout his/her life. With early diagnosis and treatment, together with parental education and involvement, affected people are living longer and surviving into middle and late adulthood.

Treatment for sickle cell disease is usually aimed at avoiding crises, relieving symptoms and preventing complications. A major part of the care of sickle cell disease can be handled at home by parents. Responsible, dedicated and knowledgeable parents do make a great difference in the outlook of their children. For some medical problems, your child will need to go to outpatient units or emergency rooms for immediate treatment. For some other more serious health problems, your child will need to be hospitalised for additional treatment and close observation. Treatments may include medications to reduce pain and fever and to prevent complications, blood transfusions and supplemental oxygen, antibiotics as well as other specific and supportive treatments. In all situations, your child will benefit mostly from care given by sickle cell disease specialists and in coordination with your child's primary care physician. Above all, your child will benefit most from your continuous involvement, knowledge and caring.

Children with sickle cell disease can lead normal lives and will grow to be healthy and productive citizens if they are offered optimal care from an early age.

Regular health care maintenance

Children with sickle cell disease must be identified through newborn screening tests and be offered special medical care early on to help prevent complications. By 2 months of age, your baby should start taking penicillin by mouth twice a day up to at least 5 years of age or as prescribed by your child's doctor. This has been shown to markedly decrease life-threatening infections. The recommended dose of penicillin is 125 mgs twice a day for children aged 2 months to 3 years and 250 mgs twice a day for those above 3 years.

Babies, children and adolescents with sickle cell disease must receive routine immunisations like their normal counterparts *(refer to **Table 1** and **Table 2** for recommended immunisation schedules for persons 0 to 6 years, and 7 to 18 years)*. Children with sickle cell disease specifically need the following vaccines: pneumococcal conjugate vaccine, 23-valent pneumococcal vaccine, Haemophilus influenzae-B vaccine, meningococcal vaccine (Mencevax®), hepatitis B vaccine and typhoid vaccine in areas endemic for typhoid fever. They also need yearly PPD (a skin test for tuberculosis) and flu shots.

Home care and regular medical checkups with a medical team experienced in comprehensive care of sickle cell disease are the main parts of sickle cell care.

Children with sickle cell disease can develop any of the common problems of childhood and need to be offered good primary paediatric care like other children.

Your child will need to make regular visits to the paediatrician or family doctor for routine health maintenance (as any other child). During these visits, your child will have a complete physical exam, undergo growth and developmental evaluation, will receive his/her immunisations and will be educated about the disease and his/her role in preventing complications. The same visits are needed for adolescents and adults with sickle cell disease. During these visits, you will have the chance to learn from your child's doctor about sickle cell disease, its danger signals and complications and home treatments for common medical problems. You will also discuss with the doctor your child's condition and issues related to your child's health (*Refer to* ***Table 3:*** *Regular health care plan by paediatrician/internist or family doctor).*

Once you are told that your child has sickle cell disease, it is advisable that he/she be enrolled in a specialised sickle cell disease centre (comprehensive sickle cell disease centre). In this centre, a team of health professionals experienced in sickle cell disease care and research will assume responsibility for your child. This team includes doctors of multiple specialties, nurse practitioners, genetic counsellors, nurses, social workers, play and occupational therapists, psychologists and dieticians. Adolescents and adults with sickle cell disease benefit greatly from enrolment in comprehensive sickle cell disease centres. During visits to these specialised centres, multiple evaluations to screen for possible disease complications will be performed for your child *(refer to* ***Table 4****: Care plan in a comprehensive sickle cell disease centre)*. New treatments as well as recent research can be discussed with you in detail.

Infections

Infections pose a great risk to your child's health and, historically, have been the commonest cause of death in children with sickle cell disease. Penicillin and immunisations have dramatically decreased the rate of these infections and deaths attributed to them. Children are more susceptible to severe infections than adults, because adults have more mature and stronger immune system than children.

Fever *can be one of the most important signs of serious infection in your child and must alert your attention as a parent.* People with sickle cell disease who have a fever must be treated the same as people who do not have their spleen. Children who have received penicillin prophylaxis and got all their immunisations may also be vulnerable to fulminant infections (ones which occur suddenly, quickly and are intense and severe to the point of lethality), but at a much lower rate than those who haven't. Fever is defined as a temperature above 100°-101°F (38.5°C) rectal, 100°F (38°C) by mouth, and 99°F (37.2°C) in the armpit (axillary). A fever above 38.5°C (101.3°F) is a medical emergency and may, if not treated promptly, result in sudden death from overwhelming infection as blood infection (sepsis). A child who has lethargy or poor skin colour or looks sick can have a serious infection, even in the absence of fever, and must be treated immediately.

So febrile or sick-looking children *with sickle cell disease must seek* ***immediate medical attention*** *and receive intensive and rapid treatment, including empiric antibiotic administration.* Acetaminophen (Panadol®, Tylenol®, Tempra®) can be given for temparatures above 101°F after calling the healthcare provider (Refer to Table 5 for acetaminophen dosage). Ibuprofen (Motrin®, Advil®, Profinal®, Pediafen®) can also be given, particularly for stubborn fever, provided the child does not have a bleeding disorder or a stomach or kidney problems (refer to Table 6 for ibuprofen dosage). Aspirin should not be given to children, as its use has been associated with a dangerous syndrome affecting the liver and the brain called Reye's syndrome.

Febrile or sick-looking children with sickle cell disease must seek immediate medical attention and receive intensive and rapid treatment, including empiric antibiotic administration.

Pain

Painful episodes or crises are the commonest manifestation of sickle cell disease at all ages. Most pain episodes are mild and can be treated at home with oral analgesia (pain killers) and non-medical therapies as massage, hot baths and distraction/relaxation methods. Acetaminophen (Tylenol®/Panadol®/Tempra®) and nonsteroidal anti-inflammatory agents (NSAIDs) such as Advil®, Motrin®, Profinal® and short acting opioids are good analgesics, and can relieve mild to moderate pain in many instances. Acetaminophen must not be given if your child has liver disease. NSAIDs should not be given if your child has any stomach or kidney disease or a bleeding disorder.

For moderate to severe pain, codeine and codeine derivatives (codeine with acetaminophen) can be used in conjunction with acetaminophen and NSAIDs. Morphine and its derivatives and morphine equivalent opioids can also be used for severe pain. Oral meperidine (Demerol®) should not be used except in very selected cases and for a short period because of its toxicity on the brain. Giving excess fluids, approximately twice your child's daily needs, can often ease the pain *(refer to* ***Table 7****: Amount of fluids needed for a person with sickle cell disease).*

On the other hand, some crises can be severe, do not respond to home management and necessitate visits to an emergency room or outpatient day treatment unit so that painkillers can be injected into your child's veins. Research has shown that outpatient day units are preferable to emergency rooms, because they provide more immediate analgesia care, and the healthcare providers in such units are more familiar with the patient's treatment schedules and experienced in screening patients for serious complications. These units have substantially decreased the rate of hospitalisation and are more convenient for patients and their families.

Encourage your child to ***drink plenty of fluids***, preferably water. This may prevent and shorten the duration of many pain crises and can prevent dehydration.

The following types of pain can be life-threatening and require immediate reporting to a doctor or a visit to the emergency room:

- Chest pain or shortness of breath
- Severe headache or limb weakness
- Severe abdominal pain with distension
- Any pain associated with severe pallor
- Joint pain, swelling and redness
- Pain refractory to home treatment
- Pain accompanied by recurrent vomiting
- Painful erection (priapism)

If outpatient treatment fails to control pain, then hospitalisation is needed, preferably in a unit which the patient is used to and where healthcare providers know your child well and have quick access to his/her medical records. In hospital, your child will receive intravenous analgesia (usually opioids as morphine) through a patient-controlled analgesia pump implanted under the skin. Through this pump, your child will control the dose and timing of his/her pain medicine by pressing a button to pump the medicine into the veins. This gives safe and good control of pain and builds up independence. While taking drugs for the pain, your child should expand his/her lungs by blowing into a balloon or into an incentive spirometer (a mouthpiece with balls inside it that the child tries to raise as high as he/she can). This lung expansion will decrease the chance of developing a lung collapse.

Stroke

Children who have had a stroke and whose tests (TCDs) show they are at high risk for developing stroke need to be treated with monthly blood transfusions for at least 5 years and, in recent studies, indefinitely. These transfusions help prevent more strokes. Treatment for minor strokes is often the same as treatment for other strokes. At the end of the treatment period, your child will undergo special studies to determine if the risk of developing a stroke in the future is still present. If this risk is still present, then transfusion needs to be continued. If not, transfusion will be stopped and the child will be monitored very carefully. Your doctor will explain the rationale and benefits of transfusion therapy in stroke and can brief you on the pioneering work of researchers in the prevention and treatment of stroke and in the treatment of transfusional iron overload.

If your child has stroke, then he/she is best treated in a comprehensive sickle cell disease centre under the supervision of an expert multidisciplinary team. This centre will offer your child neuropsychological testing and rehabilitation in addition to instructions about iron overload and chelation.

A serious outcome of sickle cell strokes and other brain problems is the development of learning problems in some affected children. To identify these learning problems early, all children should be screened with routine exams, starting at 6 years of age. If there are learning problems, they need to be managed early.

Acute chest syndrome

This extremely common complication requires hospitalisation and urgent treatment. Any delay in treatment will expose your child to unfavourable consequences. The treatment of acute chest syndrome consists of broad spectrum antibiotics given in the vein (intravenously) and by mouth in addition to medications which open up the airways (bronchodilators). Early transfusion has been shown to improve recovery and shorten hospital stay. Administration of oxygen, medications to control fever and pain and incentive spirometry to prevent lung collapse ***(atelectasis)*** are important parts of the treatment. Over-hydration is not recommended.

Acute splenic sequestration

Acute splenic sequestration is a medical emergency, and failure to recognise the symptoms and signs of this dangerous condition can result in death in few hours. The treatment of acute splenic sequestration is an immediate blood transfusion. Acute splenic sequestration can recur in a high percentage of patients, and there are various treatment options for this condition, including chronic transfusion, complete or partial removal of the spleen ***(splenectomy)***, and other potential treatments. Your child's doctor can go over all these treatment options with you, explaining their pros and cons, and together you can decide on the best option for your child.

Hand-Foot syndrome

This early sign of sickle cell disease in children is a self-limiting condition and does not leave any adverse resulting conditions (sequalae). Its treatment consists of hydration, analgesics such as acetaminophen or ibuprofen and observation. If the pain is severe and non-responsive to the usual analgesics and/or if there is fever, call your child's doctor. Your child may need hospitalisation for stronger analgesics and intravenous hydration.

Gallstones

Gallstones often result in infection in the gallbladder ***(cholecystitis)*** and sometimes in the blood ***(sepsis)***. When your child develops signs and symptoms of gallbladder infection (fever, with increasing jaundice and very yellow eyes, associated with right sided upper abdominal pain radiating to the shoulder), urgent hospitalisation and treatment with intravenous antibiotics and fluids is indicated. This is usually followed by removal of the gallbladder (cholecystectomy). The purpose of removing the gallbladder is to avoid serious and sometimes fatal complications. Taking out the gallbladder doesn't cause serious problems. Without a gallbladder, people may have trouble after eating fatty foods.

Leg Ulcers

It is important to treat leg ulcers at an early stage, when they are small and not infected. This treatment is difficult and entails good compliance from your adolescent and you. It consists of: leg-elevation, cleaning and covering the ulcer, keeping the

skin moist and wearing comfortable flat shoes and clean white cotton socks until the ulcer heals. If the ulcer is surrounded by red painful skin and there is pus oozing from it or its surroundings, indicating that it is infected, you must consult a doctor for antibiotics. If, in 2 to 3 weeks after the above treatment, the ulcer is getting larger or has not shown signs of healing, hospitalisation is required for intensive ulcer care, strict bed rest and transfusion. Transfusion brings more oxygen to the tissues and may aid healing. If despite this treatment the ulcer still doesn't heal, then a skin graft will be used to cover the ulcer. Sometimes, more than one skin graft is needed.

Avascular necrosis

Treatment of this condition depends on the patient's age and the degree of severity. Crutches are used for a period of a few weeks to a few months to take the weight off the joint. Children below the age of 12 seem to heal well with analgesia, NSAIDs and careful and limited weight bearing. As for late adolescents and adults, conservative treatment often meets with failure or partial success. Joint-preserving surgery and transfusion are often resorted to in such age groups, in order to stop joint-deformity. If your child has grown to final size and cannot walk without severe pain, hip-replacement is required.

Kidney and Bladder Problems

There are several ways you can help your child stop wetting his/her bed. You can limit the amount of fluids he/she drinks in the evening if he/she has had large amounts to drink during the day, wake him/her to urinate twice during the night, set an alarm clock in the middle of the night to wake him/her to go to the bathroom. In most kinds of kidney bleeding, it is very important to get plenty of fluids, sometimes through an IV in the hospital, and to rest in bed. After sending urine for analysis and culture, kidney infections need to be treated with antibiotics given in the vein (intravenously) for at least 10 days, and bladder infections with antibiotics given by mouth for 10 days.

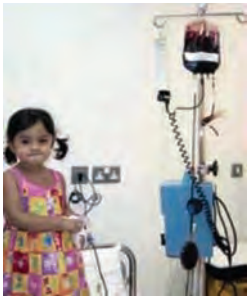
Priapism and Impotence

Priapism must be treated appropriately, because if left untreated, ***it can result in impotence over time.*** For episodes lasting for a few minutes, no treatment is necessary except for reassurance and follow-up. But for episodes lasting for hours, immediate blood transfusion should be administered. In few selected cases, surgical intervention may be needed.

Eye Problems

Sickle cell disease can cause eye-damage and, rarely, blindness. Early on, there are no symptoms and only an eye-doctor (ophthalmologist) with special equipment can see the bleeding or scarring. At this early stage, the eye-damage can be treated. Without treatment, these early changes can lead to loss of vision. It is important to be aware

that by the time your teenager complains of poor vision, changes may have gone too far. This is why your child needs to be checked by an ophthalmologist once a year.



Blood Transfusion

*Children with sickle cell disease sometimes need blood, a process called **transfusion**.* In a red blood cell transfusion, red blood cells are taken from a healthy donor and fed into one of the patient's veins. Prior to transfusion, donor blood is subjected to a battery of tests to assure its safety and its full compatibility with the blood of the patient (recipient). In sickle cell disease, blood transfusions increase the number of normal red blood cells in circulation and decrease the number of rigid sickle cells. They help to relieve anaemia and improve blood flow to tissues. In children with sickle cell anaemia at high risk of stroke, regular blood transfusions can decrease their risk of stroke. If used appropriately, transfusions can prevent or minimise organ damage and salvage many people with sickle cell disease.

There are two types of transfusions your child may get: simple and exchange. Simple transfusions are the most common. They involve giving your child a set amount of blood in the vein. An exchange transfusion involves giving your child a certain amount of blood and taking the same amount out of his/her body at the same time. This can be the best way to increase the amount of blood flowing in your child's body and decrease the number of sickle cells. Each time your child is transfused, a sample of his/her blood will be taken to determine his/her blood type (such as A positive or B negative). It is also preferable to type your child's blood for all major and minor red blood cell groups (antigens). This blood sample will be mixed with the donor's blood (of the same major and minor blood groups) to be sure the match is good.

Transfusion is indicated in the following conditions:

- Severe anemia
- Prevention and treatment of stroke
- Prolonged, painful erection of the penis (priapism)
- Lung infarction or pneumonia
- Surgery
- Frequent and severe pain

Blood transfusions do carry some risks, the commonest being iron overload. Blood contains iron, and when transfused red blood cells die, they release iron in the donor's body. With repetitive transfusion, an excess amount of iron builds up in the body, resulting in damage to the heart, liver and other organs. To avoid this complication, people who undergo regular transfusions must receive iron removal treatment ***(chelation)*** to reduce iron levels. There are several medicines that can remove excess iron and they are called chelators. Some are given under the skin, such as Desferal®, while others are given by mouth, such as deferiprone or L1. In 2005, the United States Food and Drug Administration approved deferasirox (Exjade®), an oral drug that can decrease excess iron, for use in people of all ages. This drug has

been used on a large number of people with sickle cell disease, and has been shown by researchers to be effective, safe and convenient. More studies are still needed to assure its safety in the long run, particularly in young children.

Other transfusion complications include infection with bacterial and viral germs. With proper blood screening and massive immunisations for hepatitis B, this complication is becoming less frequent. However, blood transmission of some germs that do not have a protective vaccine and are not normally screened for, such as parvovirus, is still seen and can result in severe anaemia and other sickle cell disease complications. *Some patients can also develop blood reactions* due to either a mismatch in blood groups between donor and patient or to a protein that the patient's body produces against his/her own red cells. In such cases, the patient does not benefit from the transfusion and may have worsening anaemia and sometimes fever and chills, shortness of breath, and dark urine. ***Such reactions must be treated promptly, documented and handled meticulously by the blood bank in the centre where your child has received transfusion.***

Life-threatening symptoms and signs that warrant immediate medical attention:

- T above 38.5°C or 101°F
- Weak suck and/or cry
- Marked lethargy (decreased activity)
- Chest pain and/or shortness of breath
- Sudden onset of severe headache/weakness/dizziness/ seizures
- Sudden onset of pallor
- Abdominal distension
- Sustained painful erection (priapism)
- Looking sick or toxic

New Treatments

A lot of research has been carried out in the field of sickle cell disease over the past two decades, and this has generated new and effective treatments. Such treatments have favourably changed the outlook of patients with sickle cell disease.

1. Agents which increase foetal Hb

a. Hydroxyurea (Droxia®, Hydrea®, Cytodrox®): The most promising and widely-used of these agents has been the drug called hydroxyurea. This drug seemsto work by stimulating production of foetal haemoglobin – a type of haemoglobin found in newborns that helps prevent the formation of sickle cells. This drug, usually used to treat cancer, has been proven to be very helpful for adults and children with severe disease. When taken daily, it decreases the frequency of painful crises and may reduce the need for blood transfusions. It raises the haemoglobin and improves the well-being of patients. There is some concern about the possibility that long-term use of this drug may cause tumours or leukaemia in certain people. The doctor will determine if this drug is needed and if it will help your child.

b. Butyric acid. Some studies have shown that this commonly used food additive may increase the amount of foetal haemoglobin in the blood.

2. Bone Marrow transplant
To date, bone marrow transplant offers the only potential cure for sickle cell disease. The younger the child is at the time of the transplant, the higher the cure rate and the lower the complications. In this procedure, healthy bone marrow from a donor who doesn't have sickle cell disease and who is immunologically competent with the patient is given in the vein of the patient exactly like a transfusion. This healthy marrow replaces the bone marrow and sickle cells of the patient and, after some time, starts producing normal blood cells. The patient's bone marrow is first destroyed using chemotherapy or radiation. Post-transplant, drugs to help prevent rejection of the donated marrow are given to the patient. Sometimes, the transplant doesn't work or the patient's body rejects the new marrow.

Bone marrow transplant requires a lengthy hospital stay and is quite costly. It also carries some risks and it's difficult to find matched donors. Currently, the procedure is recommended only for people who have significant symptoms and problems from sickle cell anaemia, such as those who have had stroke or severe pain and are unresponsive to all types of treatment.

3. Experimental treatments (Agents aimed at increasing water in sickle cells and decreasing stickiness of these cells)
Scientists continue to learn more about the symptoms and causes of sickle cell anaemia and to design new experimental treatments. Some of the treatments that researchers have been working on include: Clotrimazole, an over-the-counter antifungal medication which helps prevent loss of water from red blood cells and may decrease the number of circulating sickle cells. Nitric oxide, a gas that reduces red blood cell stickiness and helps keep blood vessels open, may prevent sickle cell formation. People with sickle cell anaemia have low levels of nitric oxide.

4. Gene therapy
Because sickle cell anaemia is caused by a defective gene, researchers are studying whether correcting this gene and inserting it into the bone marrow of people with sickle cell anaemia will result in normal haemoglobin formation. Scientists are also exploring the possibility of turning off the defective gene while reactivating another gene responsible for the production of foetal haemoglobin – a type of haemoglobin that prevents sickle cells from forming. This is based on the observation that patients with sickle cell disease and high foetal haemoglobin tend to have a milder course and a lower risk of complications than those with low haemoglobin F.

Suggestions for staying healthy for all age groups

- Take folic acid supplements daily, and eat a balanced diet.
- Drink plenty of water.
- Avoid temperature extremes and high altitudes.
- Avoid stress.
- Exercise regularly, but don't overdo it
- Fly on commercial airplanes with pressurized passenger cabins.

Special health issues

Teenagers

Teenagers with sickle cell disease are at risk for many problems. They run all of the risks that teenagers have, such as smoking, alcohol intake and drug addiction, plus the risks that come with sickle cell disease. These latter risks include pain crises, acute chest syndrome, stroke, gallstones, priapism, leg ulcers and avascular necrosis. Most of the healthcare needs of teenagers with sickle cell disease can be handled at home. In some cases, a visit to the doctor is needed. In othercases, hospitalisation is necessary. Teenagers with sickle cell disease need at least yearly visits to the comprehensive care centre for routine check-up and screening for organ injury.

One particular risk in this age group is the possibility of getting pregnant and having a child with sickle cell disease. Some teenagers with sickle cell disease try to get pregnant to prove that they are normal. It is important for you to reassure your daughter that she will be able to get pregnant when the time is right. You need to stress to her that teenagers with sickle cell disease who get pregnant have more problems than older women who get pregnant, and that for her, pregnancy is stressful and can be very tiring and draining. In a similar way, some teenager boys would like to show those around them that they can father children. Make sure that your teenage son knows that he can be fertile and that he and his partner need to use birth control if they want to have sex.

Use of tobacco, alcohol and illicit drugs has a significant impact on young people's health and welfare and affects all communities and their schools. Teenage is a time of experimentation and a search for identity, and can involve risk-taking – more so in patients with sickle cell disease. With drugs, smoking and alcohol, it is very important that you provide your teenager with clear guidance, and educate him/her about the risks associated with these substances. Emphasise to him/her that they can trigger pain and acute chest syndrome, and can harm the liver, kidneys, brain and other organs. Drug education must be included in teaching programmes in schools. Such education will help your teenager explore the ways in which drugs affect physical, social, mental and emotional well-being and will help him/her get support at school and in the community.

Be friendly with your teenagers, so that they feel comfortable sharing their problems with you as parents. This way, you can help solve their problems at an early stage and prevent many potentially serious complications.

Here are some tips for dealing with your teenagers:

- Tell them clearly and firmly what is acceptable and what isn't and always stick to this.
- Talk to your child from a young age about drugs, smoking and alcohol – don't wait until there's a problem.
- Talk to your daughter about the risks of pregnancy before she does something that may not be right for her.
- Encourage your teenagers to make decisions and not be mere followers, to set goals and to have high expectations and ambitions and to say 'no' to things they enjoy but are risky for them.
- Set good examples to your teenagers about drugs, smoking and alcohol. Involve them in supportive groups – sport, music, art and youth groups.

Teenager and adult Self-care
Taking steps to stay healthy is critical for adults and teenagers with sickle cell anemia. Eating well, getting adequate rest and protecting yourself from infections are good ways to maintain your health and prevent crises.

Adults

Most people with sickle cell disease can live into adulthood. As more is learned about this disease and as treatment is improving, these people are living longer and the quality of their lives is better. The most frequent complications seen in the adult group are acute chest syndrome, heart failure and renal failure. Other complications include pain, avascular necrosis, strokes, leg ulcers, painful erection (priapism) and blindness. Most of the healthcare needs of adults with sickle cell disease can be handled at home and in the local doctor's office. In some cases, hospitalisation is necessary. Adults with sickle cell disease need at least yearly visits to thecomprehensive care centre for routine check-up and screening for organ injury using laboratory and radiological studies.

Over time, almost every organ can be damaged by sickle cells. The kidneys, lungs, heart, brain, bones and eyes are particularly vulnerable. Early detection of signs and symptoms of this damage and prompt institution of proper treatment can be life saving.

Classical treatments in this age group consist of antibiotics, medications for pain control and prevention of complications, blood transfusions, supplemental oxygen and spirometry for acute chest syndrome or severe pain, and surgery for gallstones. People who develop renal failure will need transplant or dialysis. Those who develop stroke will be helped most by chronic transfusion and rehabilitation, while those who have hip necrosis will be helped by hip replacement. With frequent eye check-ups by an eye doctor experienced in sickle cell disease, blindness is unusual. Transfusions and special medicines can be helpful in cases of heart failure and acute chest syndrome. Those who are on chronic transfusion will need treatment with special medicines (chelators) to remove excess iron and prevent organ injury due to iron overload.

Adults with sickle cell disease have problems integrating into society and sometimes feel rejected by their peers. It is important to instil self-confidence and independence in them. It is also helpful to have support groups for them and to educate their society about sickle cell disease and the rights of affected people to have a happy, healthy and fulfilled life.

Adults with sickle cell disease often have fears of dying, and their parents are under the fear of losing their child at any time. This is not surprising in any chronic disease punctuated with a lot of serious health problems. If you have these feelings, share them with each other, with a healthcare provider or with a social worker or a close friend. Talking about these fears will help you to live with them. Don't let the fear of death dominate your life or your child's life.

Special school/university needs (To be met at all times)

- Getting water if thirsty
- Using bathroom when needed
- Having to make up for missing days
- Interrupting sport activities when tired
- Getting necessary medicines if needed

School/University Needs

Children and adolescents with sickle cell disease may miss many school and university days due to their recurrent health problems. Because of this, and because of poor self-esteem and coping difficulties, some of them fail their classes, get depressed and lose hope. Some others, on the other hand, do very well. School and university difficulties become more of a problem among adolescents. As a parent, it is your responsibility to share his/her school difficulties with your teenager, and to try to find appropriate solutions for them. It is important to fully inform teachers about sickle cell disease and your child's needs, and to discuss with them the difficulties he/she is facing in school. At times, you may need to consult a specialist for a possible learning disorder. Always insist on your child staying in school and setting goals and plans for a fulfilling career in the future.

Pregnancy

Women with sickle cell disease can get pregnant and deliver healthy babies. If your daughter wants to get pregnant, it is important and helpful for her to visit a genetic counsellor, who will clarify for her the chances of having a child with sickle cell disease and the various options available for having healthy children. Prior to pregnancy and during pregnancy and labour, she will need close monitoring to minimise and prevent complications for both her and her baby. Early and regular prenatal care is important. Routine pregnancy care includes a healthy diet, vitamin and folic acid supplements, increased fluid intake, stopping alcohol, smoking and medicines that can be harmful for the baby in addition to foetal growth and heart rate testing. During labour, intravenous (IV) fluids, oxygen and close foetal monitoring are needed. Close monitoring by a team of medical specialists, including an obstetrician trained in high-risk and sickle cell disease pregnancies, can help early detection and treatment of complications, resulting in a better pregnancy outcome. Complications for the

mother include high blood pressure, urinary and lung infections, gallbladder problems and heart failure. As for the baby, they are miscarriage, poor growth, premature birth and newborn death. Blood transfusion helps the blood carry more oxygen and is indicated for hypertension, severe anaemia, increased frequency of pain crises and previous foetal loss.

Surgery

People with sickle cell disease may need various types of surgery. The two commonest types are removal of the spleen (splenectomy) and removal of the gall bladder (cholecystectomy). The spleen is removed when it starts trapping blood suddenly, resulting in life-threatening anaemia (acute splenic sequestration). The commonest reason for removing the gallbladder is for gallstones. It is advised that transfusion be given prior to surgery to decrease the percentage of sickle cells. This will improve oxygenation and may minimise complications. During surgery, the patient needs to be kept warm and must receive adequate hydration. Following surgery, blowing into a small mouthpiece (spirometry) will help decrease lung collapse and lung infection, which are the two commonest complications of surgery in sickle cell disease. Early mobilisation is both needed and helpful.

Outlook for people with sickle cell disease

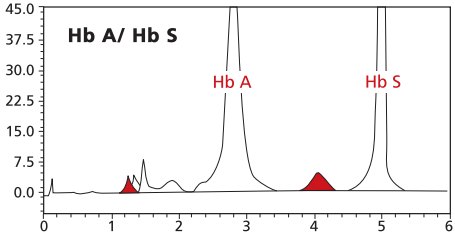
The past few decades have witnessed tremendous progress in the care of people with sickle cell disease. More recently, there is a lot of ongoing research aimed at treating and curing the disease.

The most important advances in sickle cell disease have been newborn screening, the use of penicillin, prompt treatment of infections, early diagnosis of patients at high risk for stroke, and the use of transfusions to prevent and treat stroke. Family and patient education about the disease together with compliance with doctors' advice do play an additional pivotal role in prolonging life and improving outlook. In this era, people with sickle cell disease are expected to enjoy a close to normal life and to live to late adulthood. ***Year after year, the outlook for people with sickle cell disease gets better.*** It is hoped that with the joint efforts of parents, patients, healthcare providers and researchers, ***people with this disease will have a fulfilled and full life.***

Prevention

Screening for the carrier state and the disease

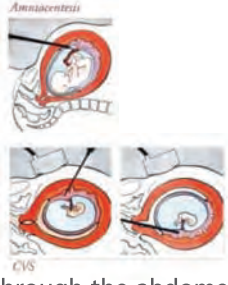
This can be done at birth by running a test called haemoglobin electrophoresis (HbE) or high performance liquid chromatography (HPLC) on a blood sample collected from the newborn's finger or heel. This same test can be used to screen older children and adults, where blood is drawn from an arm vein. This test analyses all types of haemoglobins, including haemoglobin S. If the screening test is negative, there is no sickle cell trait or disease. If the screening test shows a low percentage of haemoglobin S (less than 50%), then there is sickle cell trait (carrier). If the screening test shows a high percentage of haemoglobin S (more than 50%), there is sickle cell disease.



HPLC of a child who is a sickle cell carrier

Genetic counselling

Sickle cell carriers and sickle cell disease patients must be offered genetic counselling as soon as they are diagnosed. A genetic counsellor is a health specialist who informs people affected with inherited disorders or carrying a gene for such disorders about their future risk of having a child with a similar disorder. He/she gives information about possible treatments, preventive measures and reproductive options.



Prenatal diagnosis

This means testing a baby for sickle cell disease when the baby is still a foetus in the mother's womb. There are two ways of doing this. The first, amniocentesis, entails removing a sample of the fluid surrounding the baby through a needle inserted into the uterus between the 15th and 19th week of pregnancy. In the second method, called chorionic villus sampling (CVS), a sample of the outer placenta is removed between the 9th and 12th week, using either a needle inserted through the abdomen or a thin tube inserted via the vagina. In either method, the sample is sent for determination of the haemoglobin gene and to know if there is sickle cell disease.

Pre-implantation genetic diagnosis

This is an in vitro fertilisation procedure that improves the chances for sickle carrier parents to have a healthy child. Eggs taken from the mother and sperm from the father are fertilised in a laboratory. The fertilised eggs are then tested for the presence of the sickle cell gene. Fertilised eggs free of the sickle cell gene can be implanted into the mother for normal development. For more information on this procedure, its success rate and cost can be provided by your counselor or a specialist in the field.

Avoidance of marriage among close relatives (consanguinity)

Such a marriage, which is frequent in some countries where the disease is prevalent, increases the chances of having affected children with autosomal recessive disorders such as sickle cell disease and thalassaemia. The reason is that relatives, especially first degree relatives, are likely to have inherited from their parents similar genes, including defective ones like the sickle haemoglobin gene. In this context awareness about the potential consequences of this practice should be encouraged in countries with a high rate of marriage among relatives (consanguineous marriages).

How can you as parents help in caring for your child?

Help your child to accept the fact that he/she has sickle cell disease and to make the best of his/her life.

You are a key part of your child's healthcare team, and you need to accompany your child in all stages. Start by enrolling your child, early on, in a comprehensive sickle cell disease centre where doctors, nurses and other healthcare team members are experienced in the optimal management of this disease. It is preferable for this centre to not be very far from your home. Acquaint yourself with your child's disease at a very early stage and familiarise yourself with symptoms and signs of life-threatening events.

Your child's doctor (as well as internet websites) can educate you about sickle cell disease, its inheritance, symptoms and signs, including danger signs, complications and treatment. Take care to comply with the prescribed treatment and with the doctor's instructions, particularly regarding the need to seek immediate help when dangerous signs and symptoms become apparent.

Giving your child daily penicillin and folic acid (a vitamin needed for making new red blood cells), and making sure all vaccines are given and regular check-ups are made are important priorities. Offering your child a high calorie diet, lots of fluids and helping him/her avoid exposure to cold, high altitude and strenuous exercise are important.

As your child grows older, you have a responsibility, along with doctors, to educate your child about his/her disease, its complications and the great benefit of adhering to the prescribed treatment. *Try to involve your child in taking care of some of his/her healthcare needs.* In time, his/her role will get bigger and your role will be smaller. By teenage, he/she should be assuming control of most of his/her healthcare needs. By the time they are adults, people with sickle cell disease should be fully responsible for their own health, with their parents in the background, ready to help if needed.

Involving your child in the activities of a sickle cell disease patient group will provide a safe and fun setting ***for helping to build independence, confidence and self-esteem.*** Praise your child's assets, show him/her that you trust him/her and are confident of a well-planned, self-controlling and successful future. All along, try to be calm and supportive. Give your child self-confidence and teach him/her to carry responsibilities from a young age, gradually building up to full responsibility for his/her life and disease as he/she moves into adulthood. However, don't forget to apply the same discipline to caring for your other children and for yourself

Even though sickle cell disease is inherited and nobody can change this inheritance, nevertheless, parents can play a crucial role in early identification of infection and/or other serious problems that their children can be prone to. ***As a parent, your active role will undoubtedly contribute to a better outcome for your children, with less pain and a better and longer life.***

Common laboratory tests

When your child goes to the doctor, he/she may be sent to the lab for blood or urine tests. For a blood test, they will take some blood from the finger or the arm with a very small needle. This may hurt a little bit, but no more than a sting from an insect. It is important to tell your child that taking blood is not the same as an injection, and that it won't hurt afterwards. If a urine sample is needed, the nurse will teach you how to get it. **These are some of the most common tests:**

Haemoglobin electrophoresis (HbE)/ HPLC:
These two tests are used to find out a person's haemoglobin type and what type of sickle cell disease he/she may have. Your child will only undergo one of those tests, depending upon the doctor's discretion and the availability of the tests.

Complete blood count (CBC):
This is the most commonly ordered blood test. It gives the number, shape and size of the red blood cells and the haemoglobin level, and helps decide on the need for transfusion. Children with sickle cell disease usually have a lower haemoglobin level of 6-10 g/dl. This varies with the type of sickle cell disease. If your child's haemoglobin level is less than 6, he/she may need to be given blood or have to go to hospital. This decision is made by your child's doctor.

Reticulocyte count:
This measures young red blood cells, which are a mirror of the bone marrow activity. Bone marrow makes all types of young blood cells and releases these cells into the blood.

Urinalysis:
Urine is checked under a microscope for signs of infection or bleeding or protein. With a bacterial infection, urine is cloudy, smells bad and has bacteria and white blood cells, and sometimes red blood cells.

Other tests:
These tests measure the kidney and liver functions, amount of iron in the body (ferritin), the presence of viruses, the level of hormones, as well as the level of substances in the blood which are important for health and growth, such as glucose (sugar), and minerals.

X-Rays:
These are used to see if there is an infection in the lungs or damage to bones. They can also be used to study the age of bones, especially in children who have delayed growth.

Brain MRI:
This is mostly used to diagnose stroke.

Echo of the abdomen:
Special study used to measure liver and spleen size, to see if there are gallstones, and to measure heart function.

Echo of the heart:
Special study used to measure heart function.

Frequently asked questions

Are sickle cell carriers or those with sickle cell trait healthy?
Yes. Carriers usually don't experience symptoms unless they are in an area with low oxygen, such as at high altitude, where they may experience pain episodes or problems with their spleen. They have a higher-than-normal risk of developing urinary tract infections and may have intermittent bleeding in their urine. These problems are infrequent and do not pose any major health problem.

Can people with sickle cell trait develop sickle cell disease at any time in their life?
No. This can never happen, because those who have sickle cell trait have inherited only one sickle gene, whereas those with the disease have inherited two sickle genes. Genes are inherited from parents and are determined at conception, and thus can never be acquired in one's lifetime. Therefore, sickle cell trait can never transform into sickle cell disease.

Can people with sickle cell trait donate blood?
Yes if their haemoglobin is within normal range, which is the usual situation.

How can my partner and I be tested for sickle cell disease or sickle cell trait?
You can be tested by a complete blood count (CBC) and by either haemoglobin electrophoresis (HbE) or high performance liquid chromatography (HPLC). These tests can be ordered by your doctor and are simple and inexpensive.

What options are usually given to two sickle cell carriers who want to be marriage partners?
These two persons need to be informed about the 1 in 4 chance of having of their children affected by the disease in each pregnancy. Following that, they will be given the options. Option 1 is to reconsider and end their relationship. Option 2 is to opt not to have children and consider adopting a child. Option 3 is to accept having prenatal diagnosis in each pregnancy and opting for termination of pregnancy if the foetus has the disease. The fourth option and best option would be to do pre-implantation diagnosis, but this is an expensive option and not always successful.

If we are both carriers of sickle cell trait, can we test our baby before it is born?
Yes. Prenatal testing can be done using one of two methods, chorionic villus sampling (CVS) or amniocentesis.

Why does my child have yellow eyes?
Your child has yellow eyes due to a pigment called bilirubin, which is released from broken red blood cells. Under normal conditions, the liver gets rid of this bilirubin and the eyes are not yellow. But in sickle cell disease, the red cells are broken down much faster than usual and the liver cannot get rid of all of the excess bilirubin, which goes to the eyes and gives a yellow colour, a condition called scleral icterus. Drinking more water can help the body get rid of bilirubin in the urine and subsequently diminishes some of the yellow colour, but this can never get rid of it completely. Taking folic acid daily slightly slows down the rate at which red blood cells break down, but the yellow colour does not completely disappear.

At what age do people with sickle cell disease die?
It is a common misconception among many people, and even some healthcare providers, that patients with sickle cell disease have a very short life. The truth is that people with sickle cell disease can lead long and productive lives, with a median life span of between 40 and 60 years, and some can survive into their 70s and 80s. Those with sickle thalassaemia usually fare better than those with sickle cell anaemia. You can find a more detailed answer to this question in an article about sickle cell anaemia on the Centres for Disease Control and Prevention (CDC) website, at http://www.cdc.gov/ncbddd/sicklecell/

Is there a developmental delay in children with sickle cell disease?
Developmental delay is not characteristic of sickle cell disease, except in cases of stroke and chronic severe anaemia. However, children with sickle cell disease can develop non-sickle cell disease-related medical problems just like other children, such as brain tumour, other genetic defects, birth/prenatal hypoxia (decrease in oxygen), etc., which can result in developmental delay. In addition, they can have cognitive deficits and slightly lower IQ scores compared to non-sickle peers. On the other hand,

there are definitely adults with sickle cell disease who are intellectually brilliant and are high-powered professionals in several areas.

Can people with sickle cell disease travel by air?

People with sickle cell disease generally tolerate air travel, but they can develop some potential problems on an occasional basis, such as pain, fatigue and dehydration. The higher the altitude and the longer the trip, the more sickle cell-related problems will develop. In order to prevent these potential problems, passenger cabins must be pressurised and have the facilities to provide supplemental oxygen at all times, and excessive fluids need to be given during air travel.

Facts and myths

Myth: Only African Americans or Blacks get sickle cell disease.

Fact: Even though sickle cell disease has the highest prevalence amongst Africans, it does affect people of all racial and ethnic backgrounds. For this reason, all newborns must be screened for inherited haemoglobin disorders including sickle cell disease.

Myth: Sickle cell disease is contagious.

Fact: Sickle cell disease is an inherited disease due to a genetic defect and cannot be acquired, or transmitted and thus is not contagious. Only people born with this genetic defect can develop this disease.

Myth: If my child has the disease, it means that she or he got the sickle cell gene from both my husband and me.

Fact: If your child has the form of sickle cell disease called sickle cell anaemia, this is true. But if your child has sickle thalassaemia or sickle haemoglobin C, this is not true. In these two forms, only one parent has passed on the sickle cell gene and the other has passed on a thalassaemia or haemoglobin C gene.

Myth: Sickle cell trait is a benign condition that has no health implications at all.

Fact: Although sickle cell trait is a benign condition and those who have it enjoy a healthy life style and span, it can sometimes cause some symptoms such as pain under conditions of severe exercise, high altitude and pregnancy. Rarely, it can result in bleeding from the kidney and urinary infection. Individuals with sickle trait may have children with sickle cell disease if their marriage partner has sickle, thalassaemia, or haemoglobin C trait or disease.

Myth: People with sickle cell disease cannot get malaria.

Fact: People with sickle cell disease can get malaria, and may either die or suffer through it and survive, just like anyone else. However, people with sickle cell trait

tend to be more resistant to malaria because the trait seems to protect them from dying from malaria. This survival advantage is believed to explain the high prevalence of sickle cell disease in regions known to be endemic for malaria as Africa, the Mediterranean and Indian areas.

Myth: Nothing has changed in sickle cell treatment over the past few decades.

Fact: This is not true at all. Treatment of sickle cell disease has witnessed major improvements over the past few decades, and people with sickle cell disease nowadays have a life expectancy close to normal people.
These advances include:

- Early detection through newborn screening, followed by early penicillin prophylaxis, prompt treatment of infections and immunizations.
- Screening children for stroke risk and administering stroke-preventive therapies.
- Improving parental and patient education.
- Use of hydroxyurea, the first effective medication to improve sickle cell disease.
- Bone-marrow transplant which can cure some sickle cell disease children who are lucky to have matched sibling donors.

Myth: All sickle cell care is medical in nature and administered by doctors and other healthcare workers. The family has no role in this regard.

Fact: This is not true. Actually, a family can do a lot to care for a child with sickle cell disease. Parents and older siblings should learn about the disease, its complications and the dangerous signs necessitating emergency treatment. They should comply with doctors' instructions and take precautions to prevent or minimise pain. Parents need to support their children, give them confidence and encourage their autonomy. They are a key part of their child's healthcare team, and their active involvement has been clearly shown to decrease complications and death from the disease.

Tables

Table 1: Recommended immunization schedule for persons aged 0-6 years.
(Source: http://www.cdc.gov/vaccines/recs/schedules/child-schedule.htm)

Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2008

For those who fall behind or start late, see the catch-up schedule

Vaccine ▼ Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB	HepB		see footnote 1	HepB						
Rotavirus[2]			Rota	Rota	Rota						
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP	see footnote 3	DTaP				DTaP
Haemophilus influenzae type b[4]			Hib	Hib	*Hib*[4]	Hib					
Pneumococcal[5]			PCV	PCV	PCV	PCV				PPV	
Inactivated Poliovirus			IPV	IPV	IPV						IPV
Influenza[6]					Influenza (Yearly)						
Measles, Mumps, Rubella[7]						MMR					MMR
Varicella[8]						Varicella					Varicella
Hepatitis A[9]						HepA (2 doses)				HepA Series	
Meningococcal[10]										MCV4	

Range of recommended ages

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2007, for children aged 0 through 6 years. Additional information is available at www.cdc.gov/vaccines/recs/schedules. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations, including for **high-risk conditions:** http://www.cdc.gov/vaccines/pubs/ACIP-list.htm. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

1. Hepatitis B vaccine (HepB). *(Minimum age: birth)*

At birth:

- Administer monovalent HepB to all newborns prior to hospital discharge.
- If mother is hepatitis B surface antigen (HBsAg) positive, administer HepB and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
- If mother's HBsAg status is unknown, administer HepB within 12 hours of birth. Determine the HBsAg status as soon as possible and if HBsAg positive, administer HBIG (no later than age 1 week).
- If mother is HBsAg negative, the birth dose can be delayed, in rare cases, with a provider's order and a copy of the mother's negative HBsAg laboratory report in the infant's medical record.

After the birth dose:

- The HepB series should be completed with either monovalent HepB or a combination vaccine containing HepB. The second dose should be administered at age 1–2 months. The final dose should be administered no earlier than age 24 weeks. Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of at least 3 doses of a licensed HepB series, at age 9–18 months (generally at the next well-child visit).

4-month dose:

- It is permissible to administer 4 doses of HepB when combination vaccines are administered after the birth dose. If monovalent HepB is used for doses after the birth dose, a dose at age 4 months is not needed.

2. Rotavirus vaccine (Rota). *(Minimum age: 6 weeks)*

- Administer the first dose at age 6–12 weeks.
- Do not start the series later than age 12 weeks.
- Administer the final dose in the series by age 32 weeks. Do not administer any dose later than age 32 weeks.
- Data on safety and efficacy outside of these age ranges are insufficient.

3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP). *(Minimum age: 6 weeks)*

- The fourth dose of DTaP may be administered as early as age 12 months, provided 6 months have elapsed since the third dose.
- Administer the final dose in the series at age 4–6 years.

4. *Haemophilus influenzae* type b conjugate vaccine (Hib). *(Minimum age: 6 weeks)*

- If PRP-OMP (PedvaxHIB® or ComVax® [Merck]) is administered at ages 2 and 4 months, a dose at age 6 months is not required.
- TriHIBit® (DTaP/Hib) combination products should not be used for primary immunization but can be used as boosters following any Hib vaccine in children age 12 months or older.

5. Pneumococcal vaccine. *(Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPV])*

- Administer one dose of PCV to all healthy children aged 24–59 months having any incomplete schedule.
- Administer PPV to children aged 2 years and older with underlying medical conditions.

6. Influenza vaccine. *(Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 2 years for live, attenuated influenza vaccine [LAIV])*

- Administer annually to children aged 6–59 months and to all eligible close contacts of children aged 0–59 months.
- Administer annually to children 5 years of age and older with certain risk factors, to other persons (including household members) in close contact with persons in groups at higher risk, and to any child whose parents request vaccination.
- For healthy persons (those who do not have underlying medical conditions that predispose them to influenza complications) ages 2–49 years, either LAIV or TIV may be used.
- Children receiving TIV should receive 0.25 mL if age 6–35 months or 0.5 mL if age 3 years or older.
- Administer 2 doses (separated by 4 weeks or longer) to children younger than 9 years who are receiving influenza vaccine for the first time or who were vaccinated for the first time last season but only received one dose.

7. Measles, mumps, and rubella vaccine (MMR). *(Minimum age: 12 months)*

- Administer the second dose of MMR at age 4–6 years. MMR may be administered before age 4–6 years, provided 4 weeks or more have elapsed since the first dose.

8. Varicella vaccine. *(Minimum age: 12 months)*

- Administer second dose at age 4–6 years; may be administered 3 months or more after first dose.
- Do not repeat second dose if administered 28 days or more after first dose.

9. Hepatitis A vaccine (HepA). *(Minimum age: 12 months)*

- Administer to all children aged 1 year (i.e., aged 12–23 months). Administer the 2 doses in the series at least 6 months apart.
- Children not fully vaccinated by age 2 years can be vaccinated at subsequent visits.
- HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children.

10. Meningococcal vaccine. *(Minimum age: 2 years for meningococcal conjugate vaccine (MCV4) and for meningococcal polysaccharide vaccine (MPSV4))*

- Administer MCV4 to children aged 2–10 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups. MPSV4 is also acceptable.
- Administer MCV4 to persons who received MPSV4 3 or more years previously and remain at increased risk for meningococcal disease.

The Recommended Immunization Schedules for Persons Aged 0–18 Years are approved by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/recs/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).

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Table 2: Recommended immunization schedule for persons aged 7-18 years. *(Source: http://www.cdc.gov/vaccines/recs/schedules/child-schedule.htm)*

Recommended Immunization Schedule for Persons Aged 7–18 Years—UNITED STATES • 2008

For those who fall behind or start late, see the green bars and the catch-up schedule

Vaccine ▼ Age ▶	7–10 years	11–12 years	13–18 years
Diphtheria, Tetanus, Pertussis[1]	*see footnote 1*	Tdap	Tdap
Human Papillomavirus[2]	*see footnote 2*	HPV (3 doses)	HPV Series
Meningococcal[3]	MCV4	MCV4	MCV4
Pneumococcal[4]	PPV		
Influenza[5]	Influenza (Yearly)		
Hepatitis A[6]	HepA Series		
Hepatitis B[7]	HepB Series		
Inactivated Poliovirus[8]	IPV Series		
Measles, Mumps, Rubella[9]	MMR Series		
Varicella[10]	Varicella Series		

Range of recommended ages

Catch-up immunization

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2007, for children aged 7–18 years. Additional information is available at www.cdc.gov/vaccines/recs/schedules. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations, including for **high risk conditions:** http://www.cdc.gov/vaccines/pubs/ACIP-list.htm. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

1. Tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap). *(Minimum age: 10 years for BOOSTRIX® and 11 years for ADACEL™)*
- Administer at age 11–12 years for those who have completed the recommended childhood DTP/DTaP vaccination series and have not received a tetanus and diphtheria toxoids (Td) booster dose.
- 13–18-year-olds who missed the 11–12 year Tdap or received Td only are encouraged to receive one dose of Tdap 5 years after the last Td/DTaP dose.

2. Human papillomavirus vaccine (HPV). *(Minimum age: 9 years)*
- Administer the first dose of the HPV vaccine series to females at age 11–12 years.
- Administer the second dose 2 months after the first dose and the third dose 6 months after the first dose.
- Administer the HPV vaccine series to females at age 13–18 years if not previously vaccinated.

3. Meningococcal vaccine.
- Administer MCV4 at age 11–12 years and at age 13–18 years if not previously vaccinated. MPSV4 is an acceptable alternative.
- Administer MCV4 to previously unvaccinated college freshmen living in dormitories.
- MCV4 is recommended for children aged 2–10 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups.
- Persons who received MPSV4 3 or more years previously and remain at increased risk for meningococcal disease should be vaccinated with MCV4.

4. Pneumococcal polysaccharide vaccine (PPV).
- Administer PPV to certain high-risk groups.

5. Influenza vaccine.
- Administer annually to all close contacts of children aged 0–59 months.
- Administer annually to persons with certain risk factors, health-care workers, and other persons (including household members) in close contact with persons in groups at higher risk.
- Administer 2 doses (separated by 4 weeks or longer) to children younger than 9 years who are receiving influenza vaccine for the first time or who were vaccinated for the first time last season but only received one dose.
- For healthy nonpregnant persons (those who do not have underlying medical conditions that predispose them to influenza complications) ages 2–49 years, either LAIV or TIV may be used.

6. Hepatitis A vaccine (HepA).
- Administer the 2 doses in the series at least 6 months apart.
- HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children.

7. Hepatitis B vaccine (HepB).
- Administer the 3-dose series to those who were not previously vaccinated.
- A 2-dose series of Recombivax HB® is licensed for children aged 11–15 years.

8. Inactivated poliovirus vaccine (IPV).
- For children who received an all-IPV or all-oral poliovirus (OPV) series, a fourth dose is not necessary if the third dose was administered at age 4 years or older.
- If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age.

9. Measles, mumps, and rubella vaccine (MMR).
- If not previously vaccinated, administer 2 doses of MMR during any visit, with 4 or more weeks between the doses.

10. Varicella vaccine.
- Administer 2 doses of varicella vaccine to persons younger than 13 years of age at least 3 months apart. Do not repeat the second dose if administered 28 or more days following the first dose.
- Administer 2 doses of varicella vaccine to persons aged 13 years or older at least 4 weeks apart.

The Recommended Immunization Schedules for Persons Aged 0–18 Years are approved by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/recs/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).

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Table 3: Regular healthcare plan by paediatrician/internist or family doctor.

Age	Frequency of visits	Evaluation
Birth – 6 months	Every month	Physical exam (PE) and developmental assessment, vaccines, monthly CBC and when needed
6 months – 1 year	Every 2 months	PE and developmental assessment, vaccines, PPD and urinalysis at one year, CBC every 2 months and when needed
1 year – 5 years	Every 4 to 6 months	PE and developmental assessment, vaccines, CBC every 6 months and when needed, yearly PPD, yearly eye check-up >3 years
6-18 years	Every 6 – 12 months	PE, vaccines, CBC every 6-12 months and when needed, yearly PPD, yearly eye check-up
Over 18 years	Every year	PE, CBC every year and when needed, other tests as advised by doctor

Table 4: Care plan in a Comprehensive Sickle Cell Disease Centre

Evaluation	Interval
Physical Exam • Birth – 6 years • 6 – 18 years • Over 18 years	 Every 2 – 4 months Every 4-6 months Every 6-12 months
Family genetics	At diagnosis
Genetic Counselling and education	At diagnosis and 1-2 times per year
Social Worker visits (home, school and work site)	At diagnosis and once a year
Laboratory tests: Blood (CBC, kidney, liver tests and iron tests) and urine (urinalysis)	Every 6 – 12 months
Other special laboratory and x ray studies	When needed
Abdominal echo (to look for gallstones and spleen/liver size)	Every 2 years (>6 years) and when needed
TCD (to study stroke risk)	Once a year >2 years and more if indicated
Cardiac echo (studies heart function)	Once a year >10 years
Evaluation (eyes, lungs, neurological)	Once a year and when needed
Psychological/Family Therapy Consultation	Once a year and when needed
Physical Therapy Assessment (for joint problems and after surgery)	When needed
Developmental Screen	Once a year and when needed
Dietician	Once a year and when needed
Adolescent Centre Evaluation	At least once/year and when needed

Table 5: Acetaminophen dosage according to age and approximate weight.

		DOSAGE			
Age	**Approximate weight range**	**Oral Drops**	**Syrup**	**Chewables 80 mg**	**Chewables 100 mg**
under 3 months	Under 4.55 Kg	1/2 dropper	1/4 tsp.	-	-
3 to 9 months	8.18 – 10.45 Kg	1 1/2 droppers	3/4 tsp.	-	-
2 to 3 years	10.9 – 15.9 Kg	2 droppers	1 tsp.	2 tablets	-
4 to 5 years	16.36 – 21.36 Kg	3 droppers	1 1/2 tsp.	3 tablets	1 1/2 tablets
6 to 8 years	21.8 – 26.8 Kg	-	2 tsp.	4-5 tablets	2-2 1/2 tablets
9 to 10 years	27.27 – 32.27 Kg	-	2 1/2 tsp.	6 tablets	3 tablets
11 years	32.7 – 43.18 Kg	-	3 tsp.	6 tablets	3 tablets
12 years & over	43.64 Kg & over	-	3-4 tsp	6-8 tablets	3-4 tablets

How supplied:
Drops: Each 0.8-m1 dropper contains 80-mg acetaminophen.
Syrup: Each 5-ml teaspoon contains 160-mg acetaminophen.
Chewables: Regular tablets contain 80-mg acetaminophen each. Double strength tablets contain 160-mg acetaminophen each.
Dosage may be given every 4 hours as needed but not more than 5 times daily.
Adapted from *http://www.drelizabethdickey.com/condition.aspx?condition_id=53*

Table 6: Ibuprofen dosage according to age and approximate body weight.

		DOSAGE			
Age	**Approximate weight range**	**Oral Drops 50 mg/1.25 ml**	**Suspension 100 mg/5 ml**	**Chewables 50 mg**	**Chewables 100 mg**
5-11 months	4.55 – 7.73 Kg	1 dropper	1/2 tsp.	-	-
12-23 months	8.18 – 10.45 Kg	1 1/2 droppers	3/4 tsp.	1 1/2 tablets	1/2 tablet
2 to 3 years	10.9 – 15.9 Kg	2 droppers	1 tsp.	2 tablets	1 tablet
4 to 5 years	16.36 – 21.36 Kg	-	1 1/2 tsp.	3 tablets	1 1/2 tablets
6 to 8 years	21.8 – 26.8 Kg	-	2 tsp.	4 tablets	2 tablets
9 to 10 years	27.27 – 32.27 Kg	-	2 1/2 tsp.	5 tablets	2 1/2 tablets
11 years	32.7 – 40.45 Kg	-	3 tsp.	6 tablets	3 tablets
12 years & over	40.9 Kg & over	-	4 tsp	8 tablets	4 tablets

Adapted from *http://www.drelizabethdickey.com/condition.aspx?condition_id=53*

Table 7: Quantity of fluids needed for a person with sickle cell disease*

Body Weight (kg)	**Litres (recommended range per day)**
5	0.5 to 0.7
10	1.0 to 1.4
15	1.2 to 1.8
20	1.4 to 2.2
25	1.5 to 2.3
30	1.7 to 2.5

Body Weight (kg)	**Litres (recommended range per day)**
35	1.8 to 2.7
45	2.0 to 3.0
55	2.3 to 3.4
65	2.5 to 3.8
75	2.8 to 4.1

*(May need more with fever, pain, exercise and hot water)

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About Thalassaemia International Federation

VISION AND MISSION:

"EQUAL ACCESS TO QUALITY MEDICAL CARE FOR EVERY PATIENT WITH A HAEMOGLOBIN DISORDER"

OBJECTIVES AND GOALS:

To:

- Promote awareness about thalassaemia, its prevention and its medical and other care
- Promote and support studies and research aimed at the continuous improvement of prevention and medical care strategies, and for realizing a total cure for thalassaemia
- Collect the knowledge, experience and expertise gained from countries with successful control programmes, for dissemination to countries in need. Procure the right of every patient to equal access to quality medical care

ACHIEVEMENTS:

- Is an umbrella organization involving 98 national thalassaemia associations and other members, from 60 countries across the world
- Has entered into official relations with the Non-Communicable Diseases – Human Genetics Department of the WHO
- Is collaborating with and/or is a full or observer member of other relevant departments of the WHO, the European Commission, 30 national, 10 European and 6 international patients' organizations, 18 pharmaceutical industries and 6 health – related bodies, with an interest in haemoglobinopathies, blood safety and public health in general
- Has established an internationally recognised educational programme

EDUCATIONAL AND AWARENESS-RAISING MATERIAL PUBLISHED TO DATE INCLUDES:

1. Blood Safety Kit Manual for Patients and parents (1999);
2. Guidelines to the Clinical Management of Thalassaemia (First Edition 2000);
3. Compliance to Iron Chelation Therapy with Desferrioxamine (2001);
4. About Thalassaemia (2003) – updated in 2007;
5. Prevention of Thalassaemias and other Haemoglobinopathies – Vol I (2003);
6. Prevention of Thalassaemias and other Haemoglobinopathies – Vol II (2005);
7. "Guidelines to the clinical management of Thalassaemia" – Second Edition (2007);
8. Patients' Rights (2007);
9. A Guide to establishing a non-profit patient support organisation (2007);
10. Children's Dialogue – "Thalassaemia Major and me" – (2007);
11. Educational Booklet 1 – About Beta (β)-thalassaemia (2007).
12. Educational Booklet 2 – About Alpha (α)-thalassaemia (2007).
13. Educational Booklet 3 – About Sickle-Cell Disease (2007).
14. Educational Folder – Information for the community, the carrier of and the patient with a Haemoglobin disorder.
15. Sickle Cell Disease – A booklet for parents, patients and the community (2008)

TIF MAGAZINE is a quarterly publication, containing news and information from its members around the world and the latest scientific and medical advancements in haemoglobinopathies and other relevant fields.

Each issue is distributed to more than 4,000 subscribers in over 60 countries. Fifty two issues published to date.

A Multi-lingual DVD – About Thalassaemia International Federation (2005) - 4,000 copies distributed in 40 countries.

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