Sickle Cell Disease

Handbook for Pediatric Patients

Information and Resources

Updated 2025

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Pediatric Specialists of Virginia
Children's National
Inova Children's

Letter from Pediatric Specialists of Virginia (PSV) Sickle Cell Clinic

Sickle Cell Disease is a serious condition, but with today's medical knowledge and technology, qualify of life for children with sickle cell disease can be great. Now that your child is diagnosed with sickle cell disease, it is important to maintain consistent care with Pediatric Specialists of Virginia's (PSV) Sickle Cell Clinic, as well as with your child's pediatrician. Parents, families, and patients themselves play the most important role in the well-being of children with sickle cell disease. PSV's Sickle Cell Clinic is here to provide family-centered care and help coordinate multidisciplinary specialty care for our patients.

The Sickle Cell Team at PSV is composed of physicians, nurse practitioners, physician assistants, registered nurses, nurse coordinator, social worker, and psychologist.
Our goal is to provide comprehensive care to pediatric patients with sickle cell disease.

This booklet provides helpful information regarding the care of your child. We look forward to getting to know you and your child as we work together to provide the best sickle cell care possible.

Sincerely,

The Sickle Cell Team
Pediatric Specialists of Virginia
Center for Cancer and Blood Diseases of Northern Virginia (CCBD-NV)
Inova Schar Cancer Institute
8081 Innovation Park Drive Building B, Suite 765
Fairfax, VA 22031
571.472.1717
https://psvcare.org/northern-virginia-comprehensive-pediatric-sickle-cell-program

When to call your doctor

- Fever 100.4 F (38 C) or higher for babies younger than 6 months old
- Fever 101 F (38.5 C) or higher for children 6 months or older
- Difficulty breathing or chest pain
- Pain not relieved with home care
- Unable to hydrate
- Abdominal swelling
- Severe headache
- Sudden weakness or loss of feeling or movement
- Seizure
- Painful erection of penis lasting more than 30 minutes

When to go to the Emergency Room

If symptoms occur during normal operating hours for the Sickle Cell Clinic at Pediatric Specialists of Virginia, **please call us first at 571-472-1717**. The nurse will either get you a **clinic appointment** ASAP or arrange for an **Emergency Room** visit.

AFTER HOURS: 571-472-1717 will be routed to the Inova Fairfax Hospital operator 703-776-4000 who will page the **on-call pediatric hematologist**. Someone is available to speak with you 24 hours a day.

If you feel the child is experiencing an emergency that cannot wait for a return phone call, please do not hesitate to go to the Emergency Room. Be sure to call the on-call physician on your way at 571-472-1717.

Emergency Room	Inova Children's Hospital
Emergency Phone Number	703-776-4000 (Inova Fairfax operator)
Address	Inova Fairfax Hospital
	3300 Gallows Road, Falls Church, VA 22042

People you will meet in the clinic

The **front desk staff** will check your child into clinic and make appointments. The **medical assistants** will take vital signs, height, and weight. **Phlebotomists** will draw blood for lab tests. Some results will be available during the clinic visit.

Doctors specializing in sickle cell disease are hematologists (blood disorders specialist) who direct the medical care of your child. Sickle cell doctors will work with families to determine the best therapy for the patient. They educate the patient and family about sickle cell disease, and help each individual patient and family manage the patient's sickle cell health. PSV's sickle cell doctors are well-versed in the latest medical advances so that patients and families can benefit from new knowledge and discoveries.

The **Sickle Cell Nurse Coordinator and Educator** helps patients and families navigate the complex healthcare system. The Nurse Coordinator and Educator provides medical education, health advice, support for patients and families, and connects patients and families to needed resources, such as other specialists. The Nurse Coordinator and Educator also prepares teenagers to be more proactive about sickle cell care so that by the early 20s, young adults will be equipped with the skills and knowledge to be transitioned to adult sickle cell care, with parental support, as always.

Nurse Practitioners and Physician Assistants see patients for routine checkups and sick visits. They provide education and continuity of care. They help families understand the importance of health maintenance and assist parents along the way as the child grows.

Nurses in the clinic administer treatment and medication when your child is ill and give medical advice on the phone.

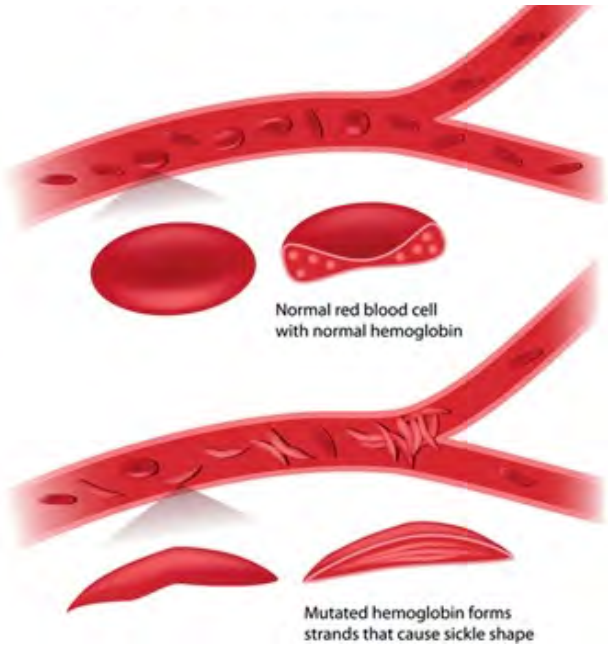
The **Social Worker** assesses the needs of patients and families, provides access to social services and community resources, assists with insurance issues, and offers support and counseling throughout the course of the child's care.

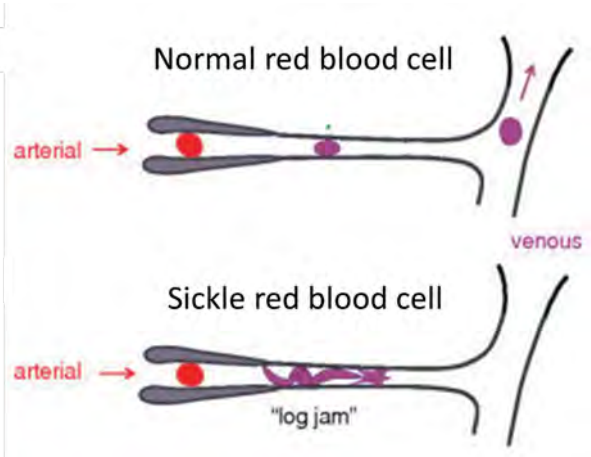
The **Psychologist** provides support and counseling for patients to help them cope with issues related to their disease or other contributing factors.

About Sickle Cell Disease

What is sickle cell disease?

Sickle cell disease (SCD) is a group of inherited red blood cell disorders. Healthy red blood cells are round, flexible, and move easily through blood vessels to deliver oxygen to all parts of the body. Oxygen is carried by hemoglobin, the main component inside red blood cells. In sickle cell disease, a mutation in hemoglobin causes the blood cells to become hard, sticky, and resemble a C-shaped farm tool called the sickle. Sickle cells break down easily, lasting only a fraction of the lifespan of a normal red blood cell, resulting in a constant shortage of red blood cells, called anemia. Because the C-shaped cells are rigid, when sickle cells travel through small vessels, they get stuck and clog the blood flow, keeping blood and oxygen from reaching parts of the body. This can cause pain in the arms, legs, chest, or back. This also causes chronic damage to all organs of the body, including the brain. Sickle cell disease is a serious condition that can be detrimental to daily life and long-term health. Fortunately, with modern medical advancements, many complications can be prevented, and children with sickle cell disease can thrive!

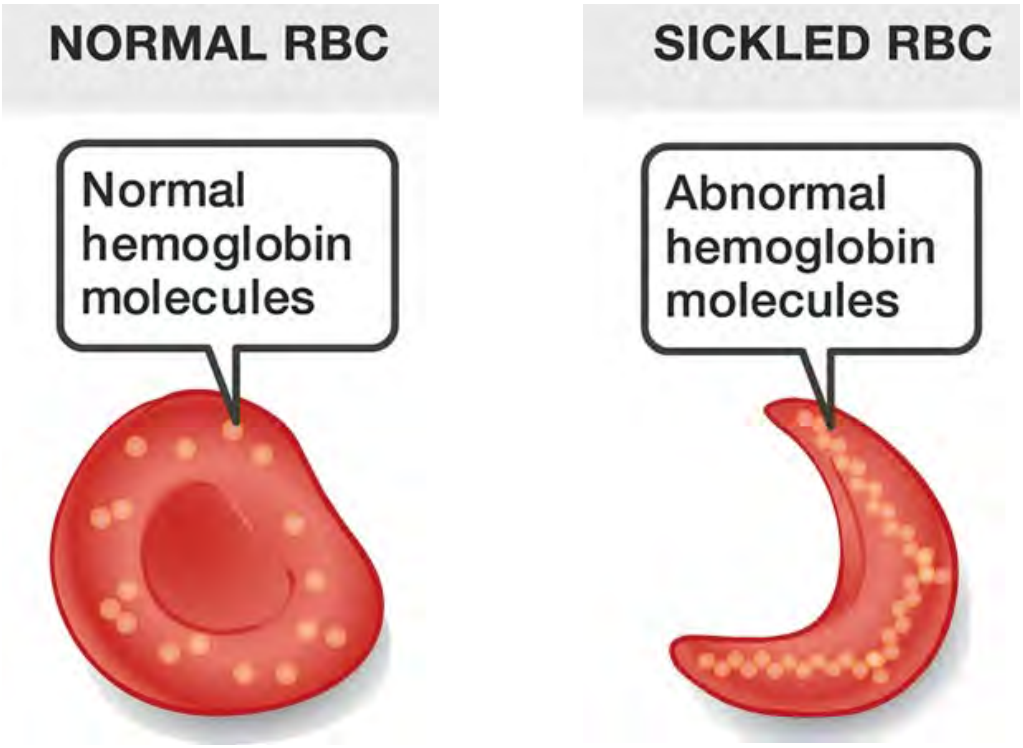




Sickle shaped red blood cells —> block blood flow —> less oxygen —> organ damage

The Sickling Problem

Hemoglobin molecules carry oxygen (O2) in the blood stream and deliver the oxygen to the tissues. The normal hemoglobin is called Hemoglobin A. The abnormal form of hemoglobin in sickle cell disease is called Hemoglobin S. When hemoglobin S molecules are not carrying oxygen, they stack to form chains, and many chains come together to form rods. The rods kink the red cell into the sickle shape. This rigid, non-deformable sickle shape clogs blood flow. **The stacking together of single hemoglobin S molecules into a chain of hemoglobin molecules, called polymerization, is the root of the problems in sickle cell disease.**



Hemoglobin S forms rods (polymerization)

Vaso-occlusion (clogging of blood vessels)

Decreased oxygen delivery

Pain, organ damage

How is sickle cell disease diagnosed?

Early diagnosis of sickle cell anemia is very important. Children who have the disease need prompt and proper treatment.

In the United States, all states mandate testing for sickle cell disease as part of newborn screening.

The baby's blood sample from a heel stick is used for all **newborn screen** tests, including sickle cell disease. The test can show whether a newborn infant has sickle cell disease or sickle cell trait.

Newborn screen results are sent to the baby's pediatrician. This is the doctor you name on the paperwork filled out at the hospital before giving birth. Parents should ask the baby's doctor for a copy of the newborn screen report.

If the test shows sickle cell disease, a second blood test is done to confirm the result. The second test should be done as soon as possible and within the first month of life. If the second test confirms sickle cell disease, the pediatrician will send you to a hematologist. This is a doctor who specializes in blood disorders. In Northern Virginia, babies with abnormal hemoglobin test results on the newborn screen are referred to Pediatric Specialists of Virginia.

Sickle cell disease can be easily diagnosed in anyone at any age, not just by newborn screening. A simple blood test called **Hemoglobin Electrophoresis** displays the type(s) of hemoglobin a person has. It is used to diagnose sickle cell disease, including the type of sickle cell disease, sickle cell trait, and other types of hemoglobin disease or trait.

Inheritance of sickle cell trait and disease

Who is at risk for sickle cell disease?
Sickle cell disease affects millions of people in the world. It is most common in people from the malaria belt, including sub-Saharan Africa, South or Central America, Caribbean islands, Mediterranean countries, Saudi Arabia, and India.

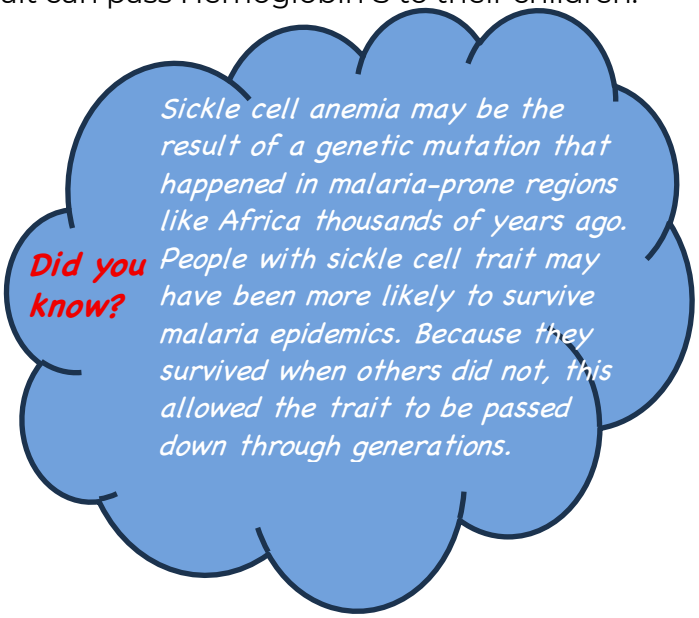
In the United States, sickle cell disease affects about 100,000 people. The disease occurs in about 1 out of every 365 African American births. Sickle cell disease also affects Hispanic Americans and occurs in 1 out of every 16,300 births. In Virginia, newborn screen identifies approximately 65 - 75 newborns with sickle cell disease annually. One in 325 African Americans in Virginia are living with sickle cell disease.

What is sickle cell trait?
Sickle cell trait is different from sickle cell disease. A person with sickle cell trait does not have the disease but has one copy of the abnormal gene that causes disease. Persons with sickle cell trait can pass the abnormal gene to their children. It takes two abnormal genes to cause sickle cell disease. In the US, about 2 million people have sickle cell trait. Sickle cell trait is detected in about 1 in 13 African American babies, 1 in 144 Latinos babies, 1 in 333 Caucasian babies, and 1 in 500 Asian or Pacific Islander babies.

Normal hemoglobin is called A. A person with 2 Hemoglobin A genes, one from each parent, has hemoglobin AA. Sickle hemoglobin is called S. A person with sickle cell trait carries one sickle hemoglobin gene (S) inherited from one parent and one normal hemoglobin gene (A) from the other parent. This person has hemoglobin AS, which is also called sickle cell trait. Persons with sickle cell trait can pass Hemoglobin S to their children.

Sickle cell trait is **NOT** a disease.
Sickle cell anemia **is** a disease.

Persons with sickle cell trait generally have no symptoms in daily life, but they can experience complications during extreme exercise at high altitudes or in low oxygen situations. Examples are professional athletes doing conditioning at high altitude cities such as Denver, and tourists traveling to high mountainous areas, such as Machu Picchu in the Andes Mountains.

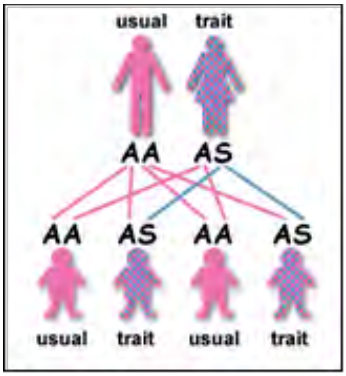


How is sickle cell disease inherited?

Everyone has two copies of the hemoglobin gene in every cell in their body, except eggs and sperm, which only carry one copy of each gene. Each person inherits one gene from their mother and one gene from their father. For a person with sickle cell trait, each egg or sperm has either the A gene or the S gene. The genes the baby gets depends on the genes carried by the egg and sperm that joined together.

Sickle cell disease is called a recessive condition, meaning you must have two abnormal hemoglobin genes to have the disorder. Sickle hemoglobin is often shortened to S or Hgb S. If you have only one copy of the sickle hemoglobin gene, along with one copy of the usual hemoglobin gene, or Hgb A, you have sickle cell trait, Hgb AS. This means you "carry" the gene and can pass it on to your children. If your partner also has sickle cell trait or sickle cell disease, then your children can inherit one copy of Hgb S from each parent and end up with two copies of the sickle hemoglobin gene, Hgb SS, and have sickle cell disease. **Genes from both parents contribute to the child's sickle cell disease.**

In the diagrams on these pages, the lines coming into each baby show that one gene coming from the mother and one gene coming from the father. Inheritance of the usual hemoglobin gene A is shown by a pink line and inheritance of the sickle hemoglobin gene S is shown by a blue line, showing 4 possible outcomes for each pregnancy. In all the diagrams, you will get the same possibilities if the genes in the mother and father are swapped.



In these diagrams, the usual hemoglobin gene is shown in pink and the sickle hemoglobin gene is shown in blue.

	A	S
A	AA	AS
A	AA	AS

Another way of showing the inheritance of sickle genes is by Punnett Square. One parent's genes are on top and one parent's genes are on in the left column. One gene on top comes together with one gene from the left column to give the baby's genes.

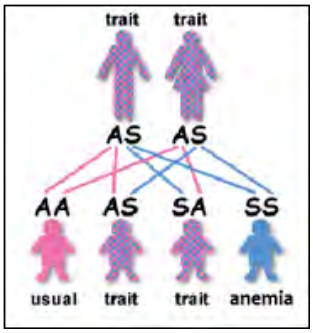
Unaffected and affected individuals

If one parent has sickle cell trait (Hgb AS) and the other does not carry the sickle hemoglobin gene at all (Hgb AA), then none of the children will have sickle cell disease. There is a one in two chance (50%) that any given child will inherit one copy of the Hgb S gene and therefore has the sickle cell trait, Hgb AS. It is equally likely that any given child will inherit two Hgb A genes and be completely unaffected, Hgb AA.

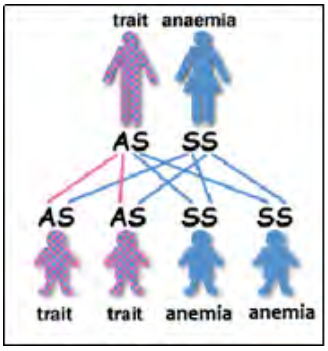
To get sickle cell disease, a child must inherit the sickle hemoglobin gene S from one parent and a sickle gene S, or another abnormal hemoglobin gene, from the other parent.

Both parents have sickle cell trait

If both parents have sickle cell trait (Hgb AS) there is a one in four chance (25%) that any given child could be born with sickle cell disease. There is also a one in four chance (25%) that any given child could be completely unaffected. There is a two in four chance (same as 1/2, or 50%) that any given child will get the sickle cell trait.



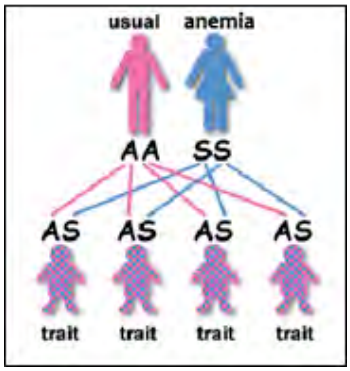
	A	S
A	AA	AS
S	AS	SS



	A	S
S	AS	SS
S	AS	SS

One parent has sickle cell trait and one parent has sickle cell disease

If one parent has sickle cell trait (Hgb AS) and the other has sickle cell disease (Hgb SS), there is a two in four chance (same as 1/2, or 50%) that any given child will inherit sickle cell trait and a two in four chance (same as 1/2, or 50%) that any given child will inherit sickle cell disease. No child will be completely unaffected.



	A	A
S	AS	AS
S	AS	AS

One unaffected parent and one parent with sickle cell disease

If one parent has sickle cell disease (Hgb SS) and the other is completely unaffected (Hgb AA), then all the children will have sickle cell trait. None will have sickle cell disease. The parent who has sickle cell disease, Hgb SS, can only pass the sickle hemoglobin gene to their children, and the parent with Hgb AA always passes on the Hgb A gene.

One parent with sickle cell trait and one parent with another abnormal hemoglobin

	A	S
A	AA	AS
X	AX	SX

Some forms of sickle cell disease result from one parent having sickle cell trait and the other parent carrying another abnormal hemoglobin, such as hemoglobin C or beta thalassemia or hemoglobin E. In this Punnett square, the abnormal hemoglobin is represented by "X." The chance of sickle cell disease in the child is one in four (25%). If one parent has sickle cell trait, then, before having children, the other parent should have his/her blood tested by hemoglobin electrophoresis for any abnormal hemoglobin, not just for hemoglobin S.

To summarize, when two people with sickle cell trait have a baby, there is:

One in four chance **(1/4, or 25%)** the baby will inherit two sickle cell genes and have **disease**.
One in four chance (**1/4, or 25%)** the baby will inherit two normal genes and **not have disease or trai**t.
Two in four chance (**2/4 = 1/2, or 50%**) the baby will inherit one normal gene and one sickle cell gene. The baby will not have the disease, but will have sickle cell trait, like the parents.

Understanding chance

To help you to think about chance, it can be useful to consider examples that we can all understand. When a woman has a baby, there is a one in two (50%) chance that the baby will be a girl and a one in two (50%) chance that the baby will be a boy. Although over the whole population there are about equal numbers of men and women, within any family there may be all girls, all boys, or a mixture of both. It is important to understand that the same chances apply to each pregnancy.

The one in two chance applies to each pregnancy. The one in two chance tells you that nature will choose one out of two different possibilities. If the chance is one in four, there are four different possibilities, and the outcome will be one of these. This is very important in understanding what your children will have if you carry the sickle hemoglobin gene. Just as there are families with all boys and families with all girls, when both parents have sickle cell trait, or one parent has sickle cell trait, and another parent has another abnormal hemoglobin, all of the children can have sickle cell disease, or all of the children can be unaffected, or there can be any combination of children with sickle cell trait, sickle cell disease, or neither disease or trait. Having had a child with sickle cell disease does not ensure the next child will not. Similarly, having had a child without sickle cell disease does not mean the next child will also not have disease. Each pregnancy is a new round of chances.

How can I find out if I carry sickle cell trait?

A simple blood test called **hemoglobin electrophoresis** can be done by your doctor or local lab. It requires that blood be taken from a vein. This is not a routine test and must be requested. The test will tell if you are a trait carrier or if you have any abnormal hemoglobin. The test will detect not only Hgb S, but other hemoglobins that can cause sickle cell disease like Hgb C, beta thalassemia, or Hgb O^{Arab}, Hgb C^{Harlem}, or others.

Pregnancy planning

If you are planning to have a baby, you and your partner can have genetic testing done. A genetic counselor or a doctor can order hemoglobin electrophoresis and DNA testing. Either a genetic counselor or a hematologist can correctly interpret the results and discuss possible risks to your children. Risk of sickle cell disease in the baby can be mitigated by in vitro fertilization and pre-implantation genetic diagnosis (IVF-PGD) (more on p.29).

Common types of sickle cell disease

Hgb SS: People who have this form of sickle cell disease inherited two sickle cell genes ("S"), one from each parent. Hemoglobin SS is the most common form of sickle cell disease and the most severe. The standard of care is to treat all children with Hgb SS with the medication **Hydroxyurea starting in infancy** to prevent sickle cell complications. Children treated with Hydroxyurea have good quality of life, similar to their peers.

	A	S
A	AA	AS
S	AS	SS

Hgb SC: People who have this form of sickle cell disease inherit one sickle cell S gene from one parent and one gene for a type of hemoglobin called "C" from the other parent. Hgb SC is usually a milder form of disease, but some children experience sickle cell symptoms. Hydroxyurea is very effective in preventing symptoms in Hgb SC.

	A	S
A	AA	AS
C	AC	SC

Hgb S beta thalassemia: People who have this form of sickle cell disease inherited one sickle cell gene from one parent and one beta thalassemia gene from the other parent. There are two types of beta thalassemia, "beta 0 (zero)" produces no Hgb A and "beta + (plus)" produces some Hgb A, but in lower amount than usual. Those with Hgb S beta 0 thalassemia have no Hgb A and have a severe form of the disease just like Hgb SS disease. Sickle beta 0 thalassemia is treated the same as Hgb SS and **Hydroxyurea** is started in infancy. People with Hgb S beta + thalassemia have a milder form of the disease.

	A	S
A	AA	AS
beta0	Abeta0	Sbeta0

	A	S
A	AA	AS
beta+	Abeta+	Sbeta+

Hgb SD, Hgb SE, Hgb SC^{Harlem}, Hgb SO^{Arab}: People who have these forms of sickle cell disease inherit one sickle cell gene and one gene of an abnormal hemoglobin. The severity of these rarer types of the disease varies. Hgb SD, Hgb SC^{Harlem}, and Hgb SO^{Arab} are similar to Hgb SS and **Hydroxyurea** is started in infancy, while Hgb SE is usually milder, similar to Hgb S beta+ thalassemia.

	A	S
A	AA	AS
X	AX	SX

Sickle cell anemia, type Hgb SS and Hgb S beta 0 thalassemia

Hemoglobin SS (Hgb SS) is the most common type of sickle cell disease. It occurs when both copies of the hemoglobin gene are S, with one Hgb S gene from each parent. People with Hemoglobin S beta 0 thalassemia (Hgb S beta 0) have one Hgb S gene and one non-functional Hgb A gene. In both of these forms, the red blood cells contain only Hgb S and no Hgb A. Red blood cells containing only Hgb S are highly susceptible to sickling, therefore Hgb SS and Hgb S beta 0 are severe forms of sickle cell disease, more specifically labeled as "sickle cell anemia," or SCA, as the blood hemoglobin is quite low when the disease is untreated, causing severe anemia.

Historically, people with sickle cell anemia were frequently sick and did not live long. Children often did not grow well and could not play or learn as children should. No treatment for sickle cell anemia was available. When patients experienced crisis, they were given opioids, or narcotics, with many side effects and negative consequences.

The past few decades saw great progress in sickle cell treatment. The discovery of Hydroxyurea as a highly effective medication, the development of curative therapies, and advances in medical care have changed the landscape of sickle cell disease. Nowadays, people with sickle cell anemia can be healthy, free of symptoms, and enjoy good quality of life as everybody else. This is especially true of children, who start protective treatment with Hydroxyurea early in life so they do not have to experience many of the complications of sickle cell anemia.

Sickle cell anemia is a serious diagnosis, and good outcome requires close adherence to therapy, regular monitoring, and vigilance of potential complications. With the help of families working closely with the sickle cell clinic, children with sickle cell anemia can grow and develop normally and thrive as their peers all the way into adulthood.

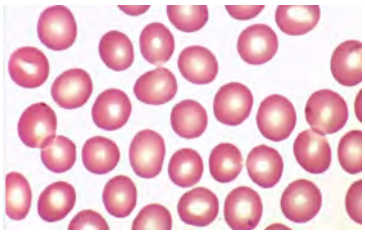
Hydroxyurea is started at 6-9 months of age. Clinic monitoring visits are monthly for 3 months when starting Hydroxyurea, then spaced to every 2 months.

Annual Transcranial doppler ultrasound (TCD) for stroke risk screening age 2 - 16.

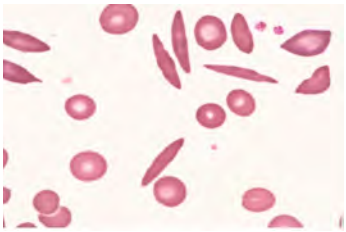
Annual urinalysis for nephropathy (kidney disease) starts at age 5.

Annual eye exam for retinopathy screening starts at age 10.

Normal blood



Sickle cell anemia blood



Sickle cell anemia, type Hgb SS and Hgb S beta 0 thalassemia – cont'd

Susceptibility to certain bacterial infections is a major concern whether a child is taking Hydroxyurea or not, and all **fevers** need to be called in and treated at a medical facility. Children with sickle cell anemia are not more susceptible to viral infections but may take longer to recover than other children. Fever illnesses can make blood counts drop, causing more severe anemia transiently. Rarely, transfusion is necessary.

Common symptoms of sickle cell anemia to watch out for are **pain**, **acute chest syndrome, splenic sequestration, aplastic crisis.**

Pain crisis in babies can show up as swelling of the fingers and toes, called **dactylitis**. In older children, sickle cell pain occurs in the long bones of the arms and legs, and the back. Many children on Hydroxyurea never experience sickle cell pain.

Any potential pneumonia is aggressively treated to avoid progression to **acute chest syndrome**, when the patient cannot get enough oxygen, which can be life-threatening. Acute chest syndrome is effectively prevented by Hydroxyurea.

Splenic sequestration occurs when the spleen acutely enlarges. Red blood cells are trapped in the spleen and hemoglobin can become very low in the circulation, causing severe anemia symptoms. Transfusion may be necessary to reverse splenic sequestration.

Aplastic crisis occurs when the bone marrow temporarily stops producing new red blood cells, usually due to infection. Hemoglobin in the bloodstream may fall very low. If the aplastic crisis does not recover in time and anemia becomes severe, then transfusion is necessary.

Other potential complications of sickle cell anemia to be aware of are listed on later pages.

Curative options

Sickle cell disease can be cured by bone marrow transplant if there is a suitable donor. For all children with sickle cell anemia who have full siblings, we test for potential match in the family for transplant, which is called HLA typing. Each full sibling has 1/4 chance of being a full HLA match. Children with Hgb SS or Hgb S beta 0 and children with mild forms of sickle cell disease but have overt sickle cell symptoms are eligible for sibling-matched stem cell transplant.

If no HLA-matched sibling is available, using one's own stem cells for gene therapy or gene editing could be an option.

Sickle cell disease, type Hgb SC

Sickle cell disease type Hgb SC is the second most common type of sickle cell disease. In each red blood cell, half of the hemoglobin is Hgb S and half of the hemoglobin is Hgb C. Hgb C by itself is benign, but Hgb S and C together cause disease. **Hemoglobin SC** is generally a **milder** form of sickle cell **disease**, but it is still disease, not trait. "Target cells" seen on blood smears is a feature of Hgb SC.

A patient with Hgb SC can have the same symptoms as the more severe forms of sickle cell disease, including pain, but usually much less frequently or not at all. Some patients are minimally affected by the disease while others have more serious complications. Regular sickle cell clinic checkups are important, regardless of symptoms. The same precautions should be taken to prevent symptoms, including staying well hydrated, avoiding extreme temperatures and low oxygen situations.

All **fevers** need to be called in and treated at a medical facility. Children with sickle cell disease may take longer to recover from an infection illness than other children. Fever illnesses can make blood counts drop, causing more severe anemia transiently.

Eye problems can occur in all types of sickle cell disease but is more frequent in Hgb SC. **Sickle cell retinopathy** and retinal detachment can cause blindness, which is a medical emergency. It is important to have the retina checked regularly by an ophthalmologist (not an optometrist who checks only the vision) who can treat retinal problems, if detected. Annual retinal exams start at age 10.

Splenomegaly, or enlarged spleen, is not uncommon in Hgb SC. **Splenic sequestration** occurs when sickle cells become trapped in the spleen causing low Hgb in the bloodstream. Severe splenic sequestration can be life threatening, but not if detected early and properly monitored and treated with transfusion if necessary.

If a patient with Hgb SC has **pain episodes** or **acute chest syndrome**, **Hydroxyurea is prescribed to prevent more episodes**. Hydroxyurea does not appear to prevent eye problems or splenic sequestration, but it does effectively prevent pain and acute chest syndrome.

Symptomatic Hgb SC patients are eligible for bone marrow transplant if a suitable donor is available.

Clinic visits every 3 months up to age 2, then every 6 months.
Blood count checks at every visit
Annual urine protein checks at age 5.
Annual retina exams starting at age 10.

Sickle cell disease, type Hgb S beta+ thalassemia

When there is one Hgb S gene and one beta+ thalassemia gene, the red blood cell contains both Hgb S and Hgb A, but the amount of Hgb A is less than the amount of Hgb S. **The presence of some Hgb A makes sickle beta+ thalassemia disease mild**.

The anemia is mild in Sickle beta+ thalassemia and hemoglobin can be near normal. A feature of beta+ thalassemia is that the red blood cells are small, which does not cause any problems and should not be mistaken for iron deficiency.

A patient with Hgb S beta+ thalassemia can be minimally affected by the disease while others have more serious complications. Regular sickle cell clinic follow up is important, regardless of symptoms. The same precautions should be taken to prevent symptoms, including staying well hydrated, avoiding extreme temperatures and low oxygen situations.

As with all patients with sickle cell disease, all **fevers** need to be called in and treated at a medical facility. Children with sickle cell disease are more susceptible to certain bacterial infections and may take longer to recover from viral illnesses than other children. Fever illnesses can make blood counts drop, causing more severe anemia transiently.

Babies with Sickle beta+ thalassemia can have **dactylitis**, which is pain and swelling of the fingers and toes. **Pain crisis** in older children involve the long bones of arms, legs, and the back. Any respiratory complaints need to be aggressively treated and monitored to avoid progression to **acute chest syndrome**. Babies are not automatically started on Hydroxyurea, but if pain or acute chest syndrome occurs, then **Hydroxyurea** is started to prevent further crisis.

If **splenic sequestration** occurs due to spleen enlargement trapping red blood cells, transfusion can reverse the process. If red blood cell production is halted leading to **aplastic crisis,** transfusion may be necessary to restore hemoglobin level. Any of the complications listed on the following pages can occur but not usually.

Bone marrow transplant is curative but is rarely necessary in Hgb S beta+ thalassemia.

Clinic visits every 3 months up to age 2, then every 6 months.
Blood count checks at every visit
Annual urine protein checks at age 5.
Annual retina exams starting at age 10.

Possible complications of sickle cell disease

This section lists many possible complications of sickle cell disease so you can be aware. It does not mean your child will experience all, or any, of them. Many patients who take Hydroxyurea consistently do not experience the complications preventable by Hydroxyurea. This is especially true of the pediatric population. Patients with mild forms of sickle cell disease often do not experience many symptoms. The goal is to prevent sickle cell complications as much as we can and to recognize symptoms as early as possible to prevent them from progressing into more serious conditions.

Anemia (low number of red blood cells or low hemoglobin): A normal blood cell has a lifespan of 3 to 4 months. A sickle cell has a life span of 1 to 2 weeks. Because of their sickled shape and rigidity, sickle cells break down, or hemolyze. The body constantly makes new red blood cells but not as fast as they are destroyed. Because of this, a person with sickle cells has fewer red blood cells and lower hemoglobin, which is called anemia. People with anemia may tire easily. Anemia means that there are not enough healthy red blood cells to carry oxygen throughout the body.

Typical hemoglobin level for **healthy non-sickle cell patient : Hgb 12–14, normal**
Typical hemoglobin level for **untreated Hgb SS or Hgb S beta O : Hgb 6–8, severe anemia**
Typical hemoglobin level for **Hgb SC or Hgb S beta+ : Hgb 10–11, mild anemia**

> **Symptoms of anemia**: fatigue, lethargy, fast heart rate, poor appetite, dizziness, irritability, pallor

When red blood cells die, the hemoglobin is broken down into something called bilirubin, which is yellow. The excess bilirubin can cause the whites of the eyes and skin to look yellow; this is called **jaundice**. Anemia and jaundice tend to be severe in untreated Hgb SS and Hgb S beta 0 thalassemia but are mitigated by Hydroxyurea. Anemia and jaundice are mild and often not noticeable in Hgb SC and Hgb S beta+ thalassemia.

Pain crisis: This is the most common symptom of sickle cell disease**.** Pain mostly in the arms, hands, legs, feet, or back happens when sickle cells plug blood vessels, blocking blood flow and delivery of oxygen to tissues. This is called vaso-occlusion. Pain due to vaso-occlusion is often called a pain crisis, also known as a vaso-occlusive crisis, or VOC.

Pain crisis in babies may present as pain and swelling in their hands or feet. This is called **dactylitis.**

How to prevent pain crisis:

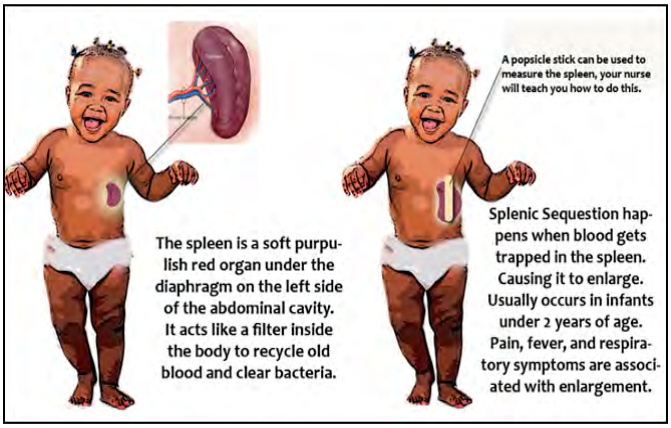
- Plentiful hydration
- Avoid extreme hot or cold (temps < 40F or > 90F) for prolonged time periods.
- Avoid places or situations with low oxygen (extreme or prolonged exercise)
- **Give your child Hydroxyurea, which is highly effective in preventing pain crisis.**

Acute chest syndrome: The condition is caused by a combination of infection and sickle cells trapped in the lungs, resulting in decreased oxygenation. Acute chest syndrome is similar to pneumonia but causes more respiratory distress. Acute chest syndrome is a major complication and can happen at all ages, including toddler age. Symptoms are usually chest pain and fever, with need for supplemental oxygen, and the chest X ray is abnormal. Sometimes transfusions are necessary to stop acute chest syndrome from worsening. Over time, lung damage from repeated acute chest syndrome may lead to chronic lung disease and pulmonary arterial hypertension. **Hydroxyurea is very effective in preventing acute chest syndrome.**

Splenic sequestration: The spleen is the organ that filters blood. In children with sickle cell disease, the spleen can enlarge rapidly from trapped red blood cells, and the amount of red blood cells in the circulation can become very low, causing severe anemia. This condition is called "splenic sequestration" and can be life-threatening. Babies and young children are at greatest risk for splenic sequestration, both in Hgb SS and Hgb SC disease. Splenic sequestration can happen as young as 3-4 months of age but more commonly between ages of 6 months to 5 years. Parents of children with sickle cell disease should learn how to feel for enlarged spleen in their child.

Symptoms of splenic sequestration:

- Lethargy
- Pallor
- Fast breathing
- Fast heart rate
- Left-sided abdominal pain and swelling
- Refusal to walk



Splenic sequestration management:

Mild cases spontaneously recover.

In more severe cases, a small transfusion releases the trapped red blood cells in the spleen back into circulation.

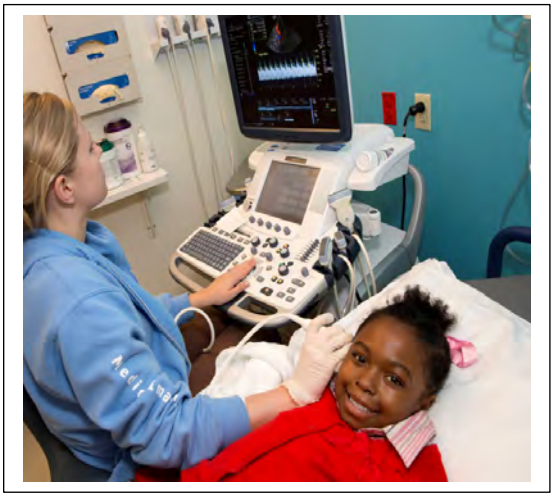
Splenic sequestration can still occur in children on Hydroxyurea therapy.

Aplastic crisis: Children with sickle cell disease may stop making red blood cells for a short time and hemoglobin may fall very low. Signs of anemia include pallor, decreased activity, fast breathing, and fast heartbeat. Aplastic crisis can occur when the child is sick with infection. A child with signs of anemia should be seen quickly by a doctor. Patients with all types of sickle cell disease can have aplastic crisis due to viral infections, especially parvovirus B19 infection.

Bacterial infections: The child with sickle cell disease is at increased risk for serious infection by certain types of bacteria, including pneumococcus and meningococcus. The risk of infection is increased because the spleen does not function normally. Fever is a sign of infection. Any time a child has fever, the child needs to be evaluated at a medical facility, blood culture needs to be drawn and an intravenous or intramuscular antibiotic needs to be administered to prevent development of sepsis (severe blood infection). Fever is the most frequent reason for ED visits in children with sickle cell disease. The most effective way to prevent severe infections is to keep up with vaccinations. Children with sickle cell disease should receive all general pediatric immunizations and additional vaccines recommended for sickle cell disease.

Hydroxyurea does not prevent susceptibility to infections, but Hydroxyurea does protect against sickle cell crisis if a child gets an infection.

Stroke: Stroke prevention is an important aspect of sickle cell treatment. Stroke happens when arteries in the brain are narrowed and/or blocked by sickled red blood cells. For children with genetically severe forms of sickle cell disease, including Hgb SS and Hgb S beta 0, a screening test called **Transcranial Doppler Ultrasound, or TCD**, is done annually starting at age 2. If this test is abnormal, your child is at risk for a stroke. In the past, these children required regular blood transfusions to prevent stroke. Now we rarely see abnormal TCD results or stroke in children taking Hydroxyurea regularly. Stroke can lead to lifelong disabilities and learning problems. **Hydroxyurea prevents abnormal TCDs.**



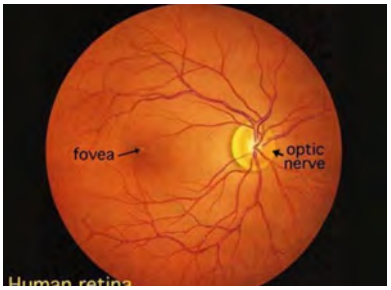
Strokes are much less frequent in milder forms of sickle cell disease, therefore, children with Hgb SC or Hgb S/beta+ thalassemia do not need routine TCDs.

Symptoms of stroke include weakness of a part of the body, facial droop, difficulty with speech, seizure, loss of consciousness. **We have not seen sickle cell strokes in children who take Hydroxyurea consistently.**

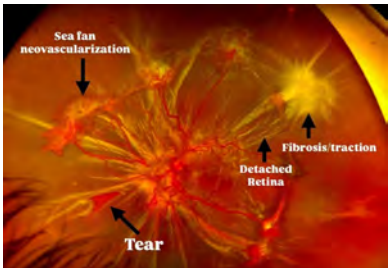
Silent cerebral infarcts (SCI) or silent strokes: These are abnormal findings on brain MRIs due to small blood vessels not delivering adequate oxygen to brain tissue. Unlike the usual overt strokes, no symptoms are associated with these small strokes, or infarcts, thus the name *silent* strokes or *silent* cerebral infarcts. Before Hydroxyurea was used for sickle cell disease, up to 30% of children with sickle cell disease had silent cerebral infarcts by school age. Whether Hydroxyurea reduces the occurrence of silent infarcts is not known.

Retinopathy: Sickle cells can also affect the small blood vessels that deliver oxygen-rich blood to your eyes. The retina is a thin layer of tissue at the back of your eyes that takes the images you see and sends them to your brain. Decreased blood flow to the retina can cause bleeding, abnormal blood vessel formation called **proliferative sickle retinopathy**, and detachment of the retina leading to blindness. Starting at age 10, patients with any type of sickle cell disease, even if taking hydroxyurea, should receive **annual monitoring retina exams**, so they can receive treatment early if abnormalities are detected. Retina monitoring is performed by an eye specialist called an ophthalmologist or a retina specialist (not an optometrist who mainly manages need for glasses or contacts) who conducts a thorough examination of your child's eyes and performs laser surgery if abnormalities are detected.

Normal retina



Sickle retinopathy



Nephropathy (kidney complication)**:** Impairment of blood flow in small blood vessels in the kidney caused by sickling of red blood cells can cause protein in the urine, blood in the urine, and tissue death in parts of the kidney called papillary necrosis. Annual urine screening begins at age 5. If protein is detected in the urine, it may be a sign of kidney damage and referral to a nephrologist, or kidney specialist, may be necessary. The kidneys of patients with sickle cell disease are not able to reabsorb water as well, and the urine is more dilute. People with sickle cell disease also produce more urine. This is another reason why hydration is important in sickle cell disease.

Gallstones: When red blood cells are broken, the hemoglobin that is normally inside the red blood cells is released into the blood stream. The body breaks down hemoglobin into a molecule called bilirubin, which is yellow, giving the appearance of jaundice. Too much bilirubin can cause bilirubin stones to form in the gallbladder. Gallstones can block the bile duct, causing pain in the upper right side of the abdomen, under the right shoulder, or between the shoulder blades. Treatment is surgical removal of the gallbladder, usually done laparoscopically. Hydroxyurea helps to keep red cells from sickling and hemolyzing (breaking down), keeping bilirubin low, which decreases the likelihood of gallstone formation.

Priapism: Males who have sickle cell disease may have painful and unwanted erections. This condition is called priapism (PRI-a-pizm). It happens because the sickle cells block blood flow out of an erect penis. Repeated priapism can damage the penis. **You must notify your doctor if you experience this.**

Avascular necrosis (AVN): Due to lack of sufficient oxygen, the tissues of some bones can die, causing pain and limitation of range of motion. Common sites of AVN are the hip joint (femoral head), shoulder joint (humoral head), and knees, as well as other less common sites. AVN is less common in the era of hydroxyurea.

Leg ulcers: Decreased blood flow to areas on the body with thin skin and not much fat under the skin, such as lower legs and ankles, can cause chronic ulcers that are difficult to heal. Hydroxyurea does not help leg ulcers. Leg ulcers are uncommon in children.

Delayed growth and puberty: Children who have sickle cell anemia who are not treated often grow more slowly and reach puberty later than other children. Children who start Hydroxyurea at an early age thrive just like other children without sickle cell disease.

Cognitive Problems: People with untreated sickle cell disease can develop cognitive (thinking) problems due to poor blood flow to the brain and decreased oxygenation. This may be hard to notice early in life. Some children may require cognitive testing and an individualized education plan (IEP) to help them be successful in school. We know Hydroxyurea helps with blood flow in the brain. Historically, children with sickle cell disease often had problems with school performance, but we see now that children treated with Hydroxyurea early in life do not tend to have school problems and can achieve as other children.

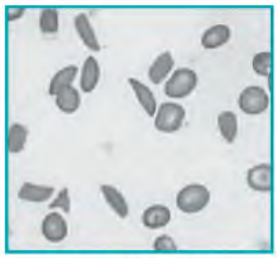
Treatment - Hydroxyurea

Hydroxyurea (HU) is a medication that improves the symptoms of sickle cell disease. It is not a cure for sickle cell disease, but can help prevent many complications, including:

- Acute chest syndrome
- Pain crises
- Trips to the hospital
- Frequent blood transfusions

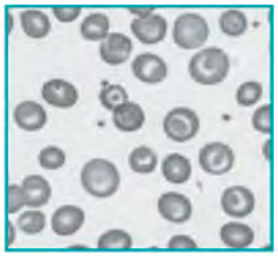
Sickle cell patients who take Hydroxyurea live longer. It is safe and beneficial to start Hydroxyurea in infancy.

Hydroxyurea must be taken as directed to help reduce sickle cell complications. It works well if taken every day as a preventive medicine. It does not work immediately and is not used as an "as needed" medicine. Hydroxyurea is taken orally in capsule form. The capsule is opened into food for young children who can't swallow the capsule.



Blood cells before taking hydroxyurea

Hydroxyurea is prescribed for anybody with severe forms of sickle cell disease, including Hgb SS, Hgb S beta 0, Hgb SD, Hgb SC^{Harlem}, Hgb SO^{Arab}, etc.



Blood cells after taking hydroxyurea

Hydroxyurea is also prescribed for people with milder forms of sickle cell disease, such as Hgb SC or Hgb S beta+, if they have symptoms, such as pain or acute chest syndrome.

How does Hydroxyurea work?

Hydroxyurea helps red blood cells stay round and flexible, so they can flow more freely in the blood stream. The drug works by **increasing the amount of fetal hemoglobin (Hgb F)** in red blood cells. Hgb F is produced naturally in fetuses but gradually turns off after birth. Hydroxyurea keeps Hgb F turned on in babies and turns Hgb F back on in older children after their Hgb F has turned off. Hgb F prevents Hgb S from sticking together and red blood cells from sickling, thus is protective against many symptoms caused by Hgb S. The higher the percentage of Hgb F, the lower the percentage of Hgb S (sickle hemoglobin), and the better it is for the patient. People with sickle cell disease who have high level of Hgb F have few or no complications. Hgb F is checked at every Hydroxyurea monitoring visit.

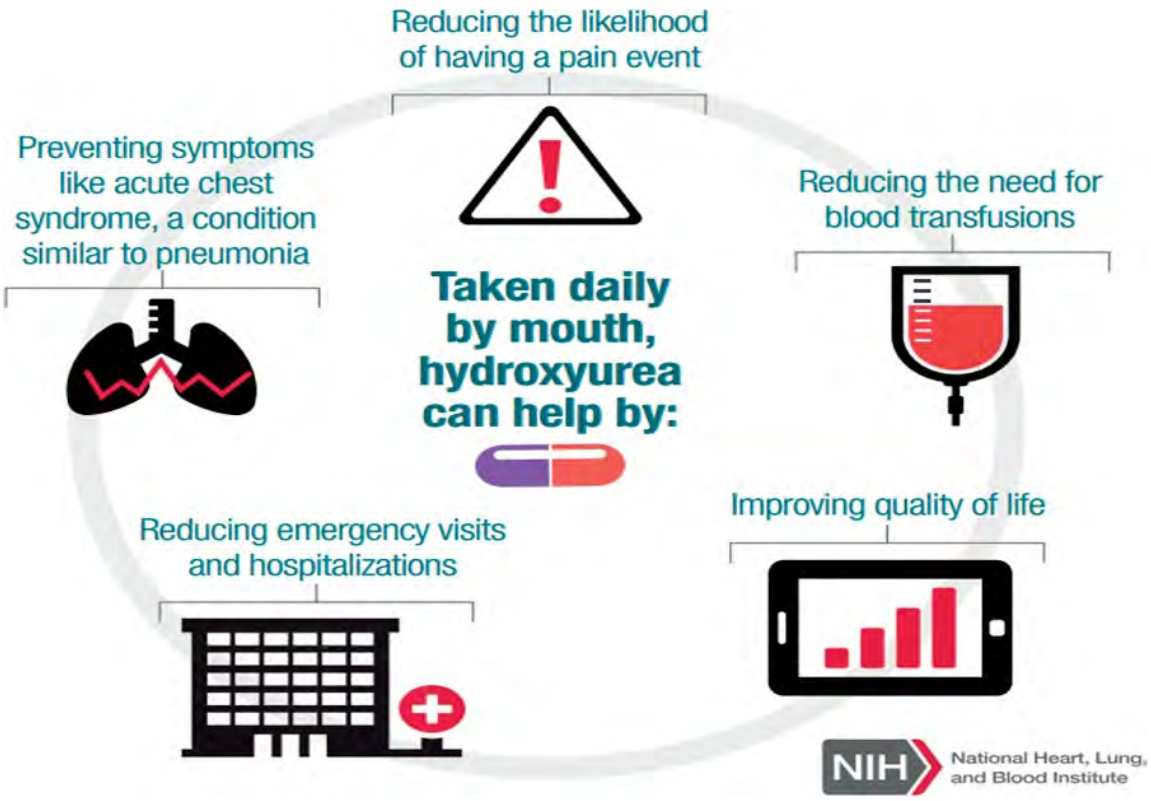
Hydroxyurea is a highly effective medicine for sickle cell disease. It is a safe medicine to take as prescribed by medical specialists treating sickle cell disease. When the dose is too low, it does not increase Hgb F enough to protect against sickle cell complications. When the dose is too high, the medicine can decrease the production of blood cells. For this reason, blood cell counts are checked regularly to optimize the dose of Hydroxyurea. Dose adjustments are expected as children grow. Hydroxyurea prevents many, but not all, sickle cell complications.

Hydroxyurea in sickle cell disease

In 1995, a large collaborative study involving 21 different sites in the US and Canada treated sickle cell patients with either placebo or Hydroxyurea. The effects of Hydroxyurea were so beneficial that the study was terminated early, and all patients were given Hydroxyurea.

- In 2010, two large studies in adults showed that **sickle cell patients who took Hydroxyurea for many years lived longer** than patients who did not take Hydroxyurea.
- In 2011, the **Baby HUG** study demonstrated that **babies with sickle cell anemia who were treated with Hydroxyurea had fewer complications than babies who were given placebo.**
- The **Baby HUG** study showed **that Hydroxyurea was safe to use in babies.**

The NIH (National Institute of Health) guideline is to start Hydroxyurea in infancy, at 6-9 months of age.

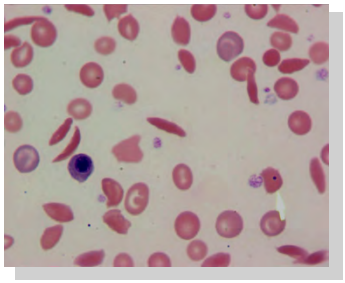


**It is important to remember, Hydroxyurea is not a cure. If you/your child stops taking Hydroxyurea, the red blood cells will begin sickling again. Even if you/your child feels great or has never had issues related to sickle cell disease, remember, it is because Hydroxyurea is working! Do not stop giving your child Hydroxyurea! **

Improvement with Hydroxyurea over time

No Hydroxyurea

- Sickle cells
- not many red cells
- Low Hgb F

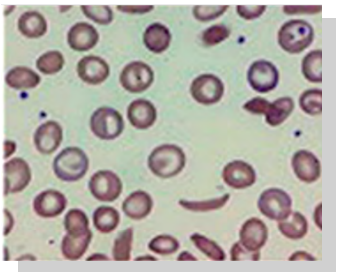


Patient status

- Fatigue
- Pain
- Acute chest

On Hydroxyurea 2 Months

- Fewer sickle cells
- Larger red blood cells
- Hgb F increasing

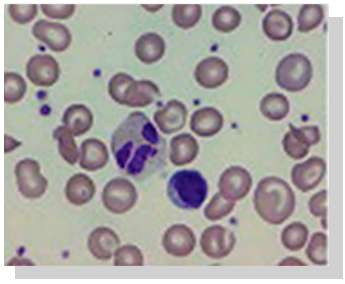


Patient status

- More energy
- Less pain
- Less frequent acute chest

On Hydroxyurea 5 Months

- Rare sickle cells
- Larger red blood cells
- High Hgb F 20-30%



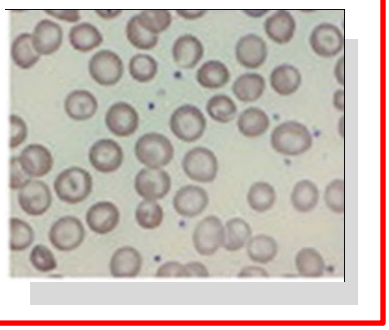
Patient status

- Increased energy
- No pain
- No acute chest
- Feels good like everybody else

On Hydroxyurea 2 Years

- No sickle cells
- All red blood cells large
- Hgb F 30% or greater

Babies' red blood cells start out beautiful like this, and we want to keep them this way by starting Hydroxyurea early before sickling begins.



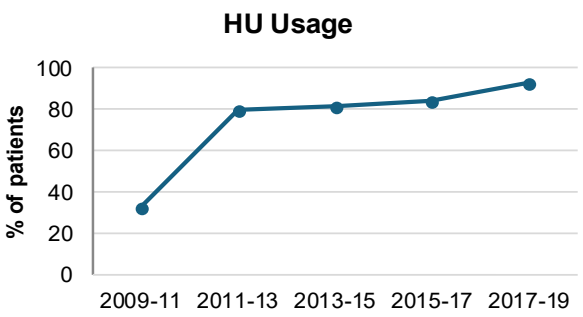
Patient status

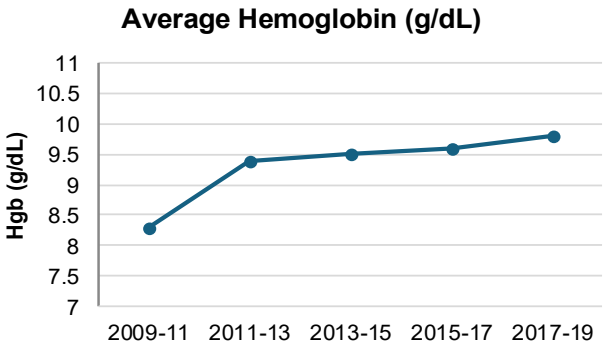
- Good energy
- Pain-free
- No acute chest
- Can't tell he/she has sickle cell disease

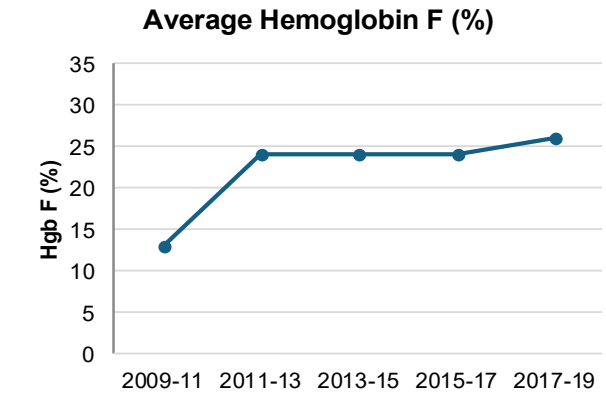
Outcomes of daily Hydroxyurea in this clinic

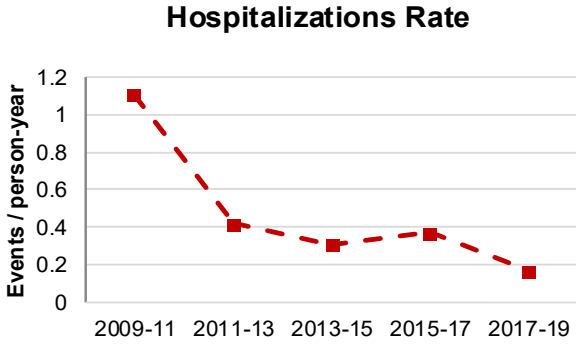
Hemoglobin increases
Hemoglobin F increases

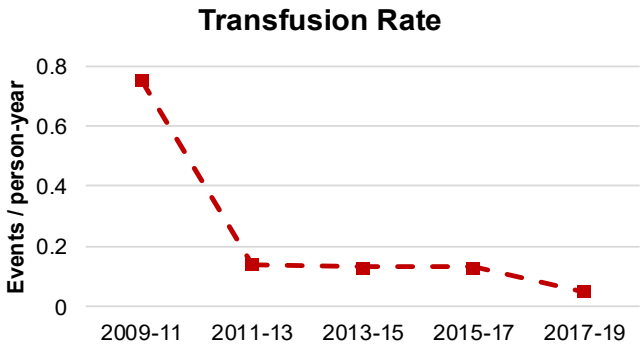
Hospitalizations decrease
Transfusions become rare
Emergency room visits are fewer

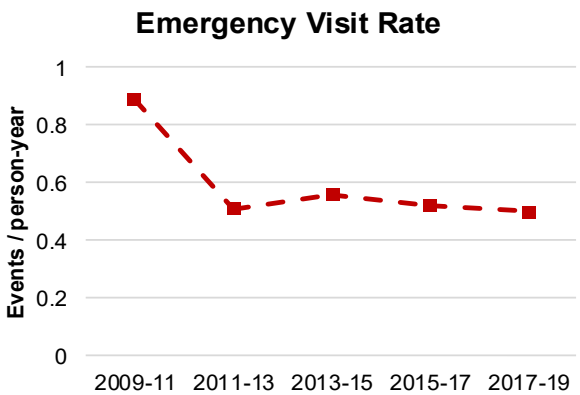












Blood transfusions

Blood transfusions are used to treat some sickle cell complications. This procedure involves transferring red blood cells collected from donors to patients.
Transfusing normal red cells to a sickle cell patient may help deliver oxygen to the body and unblock vessels. A simple transfusion gives normal red blood cells to the patient who has sickle red blood cells. An exchange transfusion removes blood from the patient while giving donor blood, replacing the patient's Hgb S-containing red cells with Hgb A-containing red cells.

Transfusions are used for:

Stroke: When a stroke occurs, the blood circulation is blocked to a portion of the brain and that part of the brain suffers damage. Transfusions are given to stop more strokes and prevent further brain damage.

Acute chest syndrome: As anemia worsens, breathing is hard and the oxygen level in the body may become too low. Blood transfusion may be needed to help oxygen delivery.

Aplastic Crisis: Sickle cells break down quickly and constant replenishment of new red blood cells is needed to keep hemoglobin up. When production of new red blood cells shuts down in an aplastic episode, hemoglobin can quickly decrease to dangerously low levels. A blood transfusion of normal red blood cells helps keep hemoglobin level up until red blood cell production resumes.

Abnormal Transcranial Doppler Ultrasound (TCD): This test uses sound waves to detect blood flow. A very fast blood flow indicates narrowed blood vessels and increased stroke risk. Hydroxyurea is very effective in decreasing TCD velocity, but if abnormalities persist, blood transfusions may be needed to decrease the risk of strokes, especially when abnormalities are seen on brain MRI/MRA.

Benefits of transfusion:

- Allows normal hemoglobin to deliver more oxygen in the body, prevents blockage of blood vessels.
- Suppresses the production of the patient's own sickle cells since transfused normal blood cells live longer than sickle cells.

Complications of transfusion:

- Development of antibodies to transfused red blood cells, making matching blood for future transfusions difficult. For this reason, patients with sickle cell disease need extensive red cell typing and should receive blood that is not only ABO matched, but also "minor antigen matched," or CEK negative.
- Too many transfusions result in Iron overload, which causes liver and other organ damage.

Infection prevention

Penicillin

Children with sickle cell disease are more susceptible to blood infections (sepsis) of certain types of bacteria due to the spleen not working properly. The spleen helps fight against these infections by removing bacteria and producing antibodies. Damage to the spleen occurs early in life due to sickle cell disease. Studies indicated that penicillin can prevent fatal cases of sepsis. When given two times each day, penicillin can kill bacteria before they grow in the blood and cause life-threatening septicemia.

Penicillin should be started once sickle cell anemia is diagnosed by newborn screen and stopped by age 5 after the child has been fully vaccinated.
Penicillin or its equivalents, such as Amoxicillin, is available in liquid, tablet, and chewable forms. The liquid penicillin must be stored in the refrigerator and discarded after 14 days.

Pneumococcal and Meningococcal Vaccines

Children with sickle cell disease are susceptible to the types of bacteria called Pneumococcus and Meningococcus. Your child should be immunized against as many strains of the Pneumococcal bacteria as possible. The pneumococcal vaccine series administered by the primary pediatricians to all children is called Prevnar, and is given at 2, 4, and 6 months, as well as a booster. It is very important that your child receives the Prevnar series on time. The sickle cell clinic gives Prevnar 20 to children who did not receive it as the primary Prevnar series. It is important that your child receives these immunizations.

There are 2 types of Meningococcal vaccines—one against serotypes A,C,W,Y and another against serotype B. Menactra or Menveo are for serotypes A,C,W,Y. and is given to all children but is given to children with sickle cell disease at a younger age with regular boosters. Meningococcal B vaccine is given to all teenagers but is given to children with sickle cell disease at age 10 as an initial 2 dose series, then as single doses every 3 years.

Influenza and COVID Vaccines: When individuals with sickle cell disease get viral infections, such as the flu or COVID, they can become much sicker than other people. Therefore, it is recommended that all children receive the flu and COVID vaccines every year. All family members should also stay up to date with flu and COVID vaccines.

Hydration

With sickle cell disease, one of the best things you can do for yourself is drink water to stay well hydrated.

Carry a water bottle with you and keep drinking water throughout the day.

Use the chart to the right to guide you on the amount of water you should drink every day.

Dehydration (not having enough water in the body) can be caused by:

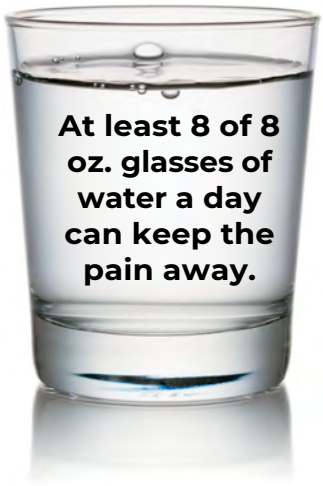
- Sweating in hot weather or during exercise
- Diarrhea or vomiting
- Frequent urination (sickle cell disease damages the kidneys, causing them to produce more urine than usual)
- Drinks with high caffeine (soda, energy drinks) and alcohol cause dehydration and are not a good idea.

Body Weight	Number of 8 oz. glasses of water needed
10 pounds	2-3
25 pounds	4-6
30 pounds	5-8
45 pounds	6-9
55 pounds	7-10
75 pounds	8-11
100 pounds	9-13
130 pounds	10-15
150 pounds	11-17
175 pounds	12-18

Tired of water? Add these to your hydration

- Fruit
- Milk
- Crystal Light drink mix
- Soup
- Gatorade
- Popsicles

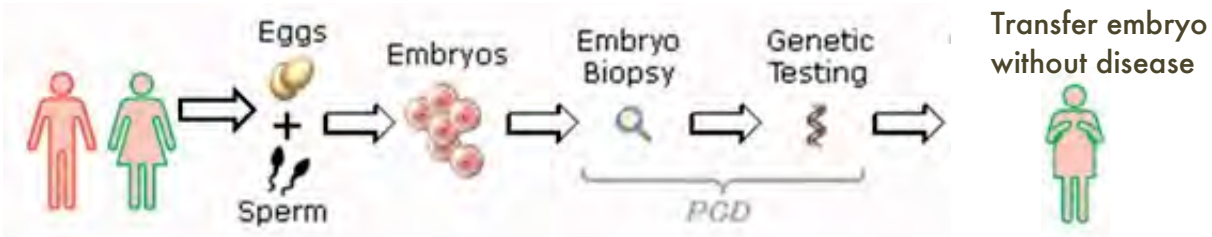
Avoid energy drinks!
These contain large amounts of caffeine and artificial sugars.
People with sickle cell disease have been admitted to the hospital after consuming energy drinks!



Can sickle cell disease be prevented?

Sickle cell disease is a genetic disease, meaning that it is inherited from parents who are carriers. For people who are carriers, or who have the trait, and are planning to have children, a hematologist or genetic counselor can help you understand your chances of having a child with disease and explain the choices available to you. One way to ensure a baby will not have sickle cell disease if both parents are carriers is through in-vitro fertilization. Sperm and eggs are collected and fertilization occurs in the laboratory for embryos to form. Testing can determine if an embryo has sickle cell disease or not. An embryo that does not have sickle cell disease is then implanted into mom's uterus to develop into a baby. A person with sickle cell disease who has a partner with sickle cell trait can also use this process to ensure having healthy babies without sickle cell disease. This process is called IVF-PGD, or in vitro fertilization-preimplantation genetic diagnosis.

IVF/PGD – in vitro fertilization and preimplantation genetic diagnosis



Can sickle cell disease be cured?

Bone Marrow Transplant

Blood cells are produced in the bone marrow. Bone marrow from a healthy donor transplanted into a patient with sickle cell disease can cure the disease in the recipient. It works best in young patients who have a full sibling donor. These are called **HLA-identical** or **match related donor (MRD)** transplants. Transplants can also be done using donors other than a matched sibling. Transplants using half-matched donors, including parents or siblings with half matched HLA types, are called haplo-transplants. Transplant procedures are always improving and becoming less toxic. We screen full siblings of our sickle cell patients to see if there is a match for stem cell transplant.

These are the ideal criteria for standard bone marrow transplant:

- Bone marrow donor is a full sibling.
- Sibling is a full HLA match.
- Donor cannot have sickle cell disease but can have sickle cell trait.

Umbilical Cord Blood Banking

If you have a child with sickle cell disease and you are pregnant again with a full sibling of the child with sickle cell disease (same mother and same father), it is possible that the new sibling is a full HLA match with the child with sickle cell disease and can be a donor for curative transplant for the affected sibling. The umbilical cord contains stem cells which can be used together with bone marrow stem cells to augment transplant in the future. Cord blood banking is a way of storing newborn stem cells from umbilical cord. After the new baby is born, we will test the baby to see if the baby is HLA matched with the sibling with sickle cell disease. If so, cord blood is already stored. A cord blood bank called ViaCord has a program called Sibling Connection. The Sibling Connection program allows for free storage of cord blood for up to 5 years for a sibling of a child with a proven genetic disorder, such as sickle cell disease.

For more information, visit https://www.viacord.com/cord-banking/sibling-connection or call 1-866-668-4895.

THE SIBLING CONNECTION

ViaCord's Newborn Stem Cell Donor Program

New curative therapies

Gene Therapy

In December 2023, FDA approved gene therapy for sickle cell disease. Stem cells are collected from the bone marrow of the person with sickle cell disease. A gene for Hgb A is inserted into these stem cells, and the genetically modified stem cells are infused back into the patient to make red blood cells that contain Hgb A.

Gene Editing/CRISPR

In December 2023, FDA also approved gene editing for sickle cell disease. Stem cells are collected from the bone marrow of the person with sickle cell disease, and a technique called CRISPR is used to "turn on" the fetal hemoglobin gene to make red blood cells have more Hgb F without the need for Hydroxyurea.

Ongoing studies are using gene editing to “correct” the Hgb S gene back into Hgb A gene.

Both gene therapy and gene editing/CRISPR are auto-transplantation processes and require clearing the body of the original bone marrow before infusion of the newly modified stem cells, a step that has associated toxicities. These genetic therapies are options for patients without donors for conventional bone marrow transplant.

Clinical Trials

Clinical trials are always taking place. To find out more about which trials are going on to find new treatments for sickle cell, visit www.clinicaltrials.gov

A child cured of sickle cell after a BMT with his sibling as a donor.

Photo credit: http://curesicklenow.org/more-stars/http://curesicklenow.org/more-stars/

Monitoring labs

- **How are blood test results different in patients with sickle cell disease?**
- **What lab work is monitored on Hydroxyurea treatment?**
- **What do lab results mean?**

Blood counts in sickle cell anemia

SCA: Sickle cell anemia, includes Hgb SS, S beta 0 thalassemia, Hgb SC^{Harlem}, SO^{Arab}, etc., which are genetically severe forms of sickle cell disease.

Labs at clinic visits:
CBC : complete blood count
retic count : new RBCs
Hemoglobin F : fetal hemoglobin, which is protective

Examples of CBC

Component	No SCA	SCA before HU	SCA after HU	Look for these changes in blood work
WBC 4.29 - 11.20 x10 3/uL	8.73	14.43 (H)	6.14	White blood cell count high in SCA due to inflammation, lower inflammation, and lower WBC with HU
Hemoglobin 10.6 - 13.3 g/dL	12.6	7.7 (L)	10.3	Hemoglobin low in SCA from sickle cells breaking down. HU protects red blood cells and increases hemoglobin
Hematocrit 32.3 - 39.7 %	35.8	21.6 (L)	27.8 (L)	
Platelet Count 203 - 368 x10 3/uL	269	523	156	Platelet count high in SCA due to inflammation. HU lowers inflammation and platelet count
RBC 3.93 - 5.00 x10 6/uL	4.25	2.49 (L)	2.62 (L)	
MCV 75.2 - 86.9 fL	84.2	86.7	106.1 (H)	HU increase red blood cell size, making them plump and juicy, less likely to sickle
MCH 24.8 - 29.4 pg	29.2	27.2	39.3 (H)	
MCHC 32.0 - 34.8 g/dL	33.9	33.0	37.1 (H)	
RDW 12 - 14 %	12	23 (H)	16 (H)	
MPV 8.9 - 12.5 fL	8.8	9.1	10.3	
Neutrophils None %	48.2	61.2	22.4	
Nucleated RBC 0.0 - 0.0 /100 WBC	0.0	4.9 (H)	0.5 (H)	
Neutrophils Absolute Count (ANC) 1.64 - 7.71 x10 3/uL	4.21	8.81 (H)	1.38	ANC high in SCA due to inflammation, comes back down with HU
Nucleated RBC Absolute 0.03 - 0.11 x10 3/uL	0.0	0.71 (H)	0.03	
Reticulocyte Count Automated 1.0 - 1.9 %	1.2	24.0 (H)	5.7 (H)	High % of new red cells in SCA, working hard to replace lost sickle cells; HU prevents sickling, less RBC loss, retic lower
Hemoglobin F (fetal hemoglobin) 0.0 - 2.0 %	2.0	5.4	32.1	HU raises fetal hemoglobin to protect red blood cells from sickling. Needs to be 20-30% to be effective. 30% or higher is best.
Bilirubin Total 0.2 - 1.4 mg/dL	0.4	5.5 (H)	1.4	Broken sickle cells release bilirubin, causing jaundice; HU prevents red blood cell destruction, decreasing bilirubin, no more jaundice

Blood counts in
Hgb SC and Hgb S beta+ thalassemia, Hgb SE

Labs at clinic visits:
CBC : complete blood count
retic count : new RBCs

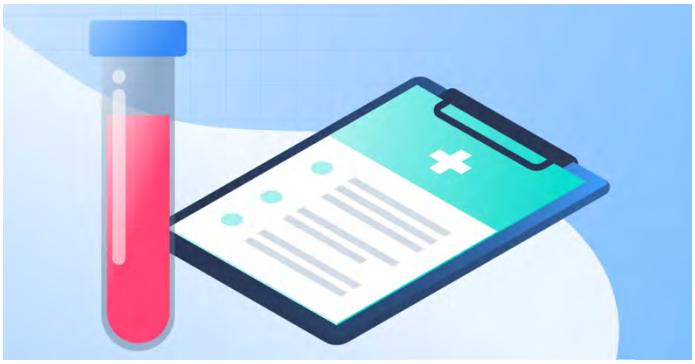
Diagnostic test:
Hemoglobin electrophoresis: displays types of hemoglobins

In mild forms of sickle cell disease, including Hgb SC, Hgb S beta+ thalassemia, or Hgb SE, Hgb is usually just a little bit lower than normal ~ 10 – 11, retic usually 2-5%. MCV is lower than normal, usually between 60-70. Bilirubin varies, from normal to slightly high.

Examples of CBC

Component Latest Ref Rng	No SCD	Hgb SC	Hgb S beta+	Hgb SE	
WBC 3.50 - 9.92 x10 3/uL	**6.95**	6.52	5.2	5.94	
Hemoglobin 11.6 - 14.9 g/dL	**13.0**	**10.4 (L)**	**10.1**	**12.0**	Hemoglobin 1-2 g/dL lower than normal
Hematocrit 33.2 - 45.3 %	**39.2**	**29.0 (L)**	**30.0**	**33.5**	
Platelet Count 151 - 380 x10 3/uL	238	204	271	300	
RBC 3.81 - 5.41 x10 6/uL	4.98	4.09	4.36	5.02	
MCV 76.0 - 94.8 fL	**80**	**70.9 (L)**	**68.8**	**66.7**	Red blood cells are small
MCH 25.2 - 32.8 pg	25.2	25.4	23.2	23.9	
MCHC 31.5 - 36.6 g/dL	33.2	35.9	33.7	35.8	
Reticulocyte Count 0.9 - 1.5 %	1.2	**2.4**	**2.8**	**1.6**	Slightly higher % of new red cells due to mildly increased red cell destruction
Bilirubin Total 0.2 - 1.4 mg/dL	0.7	**2.3 (H)**	**1.8**	**0.6**	Lysed red cells release hemoglobin, which is converted to bilirubin

Interpreting lab results



Complete blood counts (CBC) lists Hemoglobin (Hgb), Mean Corpuscular Volume (MCV), platelet count, White blood cell count (WBC), and Absolute Neutrophil Count (ANC).

Hemoglobin (Hgb) is the molecule inside red blood cells that carries oxygen throughout the body. When sickle red blood cells break down, hemoglobin is lost and oxygen carrying capacity is low. The hemoglobin level is tracked at each clinic visit to make sure that your hemoglobin is stable and in safe range.
The medication Hydroxyurea decreases sickling, which helps to raise the hemoglobin and the oxygen carrying capacity in the body.

Reticulocytes (retic) are new red blood cells that enter the bloodstream from the bone marrow. If you have sickle cell disease, you may have a higher reticulocyte count because your body is working hard to make more red blood cells to replace lost cells. People with sickle cell anemia have high reticulocyte counts. As the Hgb rises with treatment (such as Hydroxyurea), retic count becomes lower as fewer cells are lost and the bone marrow no longer needs to work so hard to make up for low Hgb.

Mean Corpuscular Volume (MCV) is the average volume, or size, of red cells. Children with Hgb SS usually have normal values, while children with Hgb S beta thalassemia, Hgb SC or Hgb SE have lower MCV, because their red blood cells are smaller. Some children might have lower MCV due to iron deficiency, which is not the reason for small cells in Hgb SC or Hgb S beta thal. When we place children on the medication Hydroxyurea, the red blood cells become larger (plump and juicy) and the MCV becomes higher, which makes the red blood cell less likely to sickle. We look for high MCV in patients taking Hydroxyurea.

Absolute Neutrophil Count (ANC) is the number of neutrophils in the blood. A neutrophil is a type of white blood cell that helps fight bacterial and fungal infections. In untreated sickle cell disease, white blood cell and neutrophil counts are very high, which reflect inflammation that makes vaso-occlusion worse. Hydroxyurea decreases ANC, which is good, but we do not want to drop the ANC too low, so this value is routinely checked. We aim to keep ANC > 1.0 (1000).

Bilirubin (bili) is yellow and causes jaundice. Hemoglobin that spills out from destroyed sickle cells turns into bilirubin. Children with untreated sickle cell disease and lots of red cell breakdown have high bilirubin and jaundiced eyes. If sickle cell anemia is treated, such as with Hydroxyurea, red blood cells do not sickle and break as much, the hemoglobin stays inside the red blood cells, no bilirubin is produced and the eyes stay clear without jaundice.

Fetal hemoglobin (Hgb F) is the hemoglobin in the fetus and helps carry oxygen from the mother's bloodstream to tissues in the fetus. After the baby is born, the amount of fetal hemoglobin gradually drops as the baby starts to make the adult form of hemoglobin (Hgb A or Hgb S). Hgb F interferes with sickling (or Hgb S polymerization), so high Hgb F is protective against sickle cell symptoms. Hydroxyurea works by increasing Hgb F. We dose Hydroxyurea to achieve high Hgb F. Hgb F level is checked at every clinic visit. Hgb F 30% or higher is best.

Hemoglobin electrophoresis is the test that displays all the hemoglobin types in a person, including Hgb A, Hgb S, Hgb C, Hgb E, etc. In patients with Hgb SS or Hgb S beta 0, there is 0% Hgb A. In Hgb SC, there is approximately half Hgb S and half Hgb C, no Hgb A. In Hgb S beta+ , there is 60-70% Hgb S and 20-30% Hgb A. In sickle cell trait, there is ~ 60% Hgb A and ~40% Hgb S. Hemoglobin electrophoresis is the test to diagnose any type of hemoglobin disease or trait. This is the test to do for partner testing.

Clinic monitoring

For sickle cell health, it is important to come to sickle cell clinic regularly. There are monitoring and preventive measures that guard against expected and unexpected complications. Even if your child is not displaying sickle cell complications that you can see, it is still important to maintain sickle cell clinic visits to make sure all immunizations and screening tests are up to date, to keep up with sickle cell education and to keep updated on new information.

Standard clinic monitoring visits for patients on Hydroxyurea therapy is every 2 months. Standard followup visits for patients with mild forms of sickle cell disease is every 6 months. Checkup intervals are adjusted as necessary.

Patients who come to clinic regularly do better with their sickle cell disease.

Pediatric Sickle Cell Clinic Health Maintenance Schedule

Hgb SS, Hgb S beta 0 thalassemia, or other genetically severe forms of SCD

Penicillin or Amoxicillin prophylaxis, age 0-5 years

Start Hydroxyurea at 6-9 months of age. Monthly visits x 3 when initiating Hydroxyurea.

Clinic visits every 2 months for Hydroxyurea monitoring. CBC, retic, Hgb F every visit. CMP annually.

TCD (Transcranial doppler ultrasound) annually age 2-16

Hgb SC, Hgb S beta+ thalassemia, Hgb SE, or other genetically mild forms of SCD

Clinic visits every 3 months age 0-2

Clinic visit every 6 months after age 2. CBC retic every visit

If symptomatic, start Hydroxyurea. Monthly visits x 3 when initiating Hydroxyurea, then every 2 months

All sickle cell disease types

Annual urinalysis starting at age 5

Annual random urine microalbumin starting at age 10. If abnormal, test first morning urine.

Annual eye exams by ophthalmologist to screen for sickle cell retinopathy starting at age 10.

Immunizations in addition to general pediatrics vaccines

Pneumococcal: Prevnar 20 as the primary series. If other pneumococcal vaccines were received as primary series, then need to make up at least one dose of Prevnar 20

Meningococcal ACWY: Menveo at 9 months and 12 months, then every 5 years

Meningococcal B: 2 doses initial series at age 10, then every 3 years

Influenza vaccine: annually

COVID vaccine: annually, or as directed by CDC

Sickle Cell Organizations and Resources

Pediatric Specialists of Virginia Sickle Cell Program
Inova Schar Campus
8081 Innovation Park Dr. Suite 765, Fairfax, VA 22031
571-472-1717
https://psvcare.org/northern-virginia-comprehensive-pediatric-sickle-cell-program

Virginia Department of Health/VDH
P.O. Box 2448
Richmond, Virginia 23218-2448
109 Governor Street
Richmond, Virginia 23219
https://www.vdh.virginia.gov/sickle-cell-programs/

Center for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329-4027
800.CDC.INFO (800.232.4636) / TTY: 888.232.634
https://www.cdc.gov/sickle-cell/index.html

National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892
301.496.4000 / TTY: 301.402.9612
NIHinfo@od.nih.gov
https://www.nhlbi.nih.gov/health/sickle-cell-disease

Sickle Cell Information Center
Emory Center for Digital Scholarship
201 Dowman Drive
Atlanta, Georgia 30322 USA
404-727-7857
http://www.scinfo.org

Faces of Our Children
1920 L Street, NW, Suite 301,
Washington, D.C. 20032
Phone: 1-866-FACES11
http://www.facesofourchildren.org

Sickle Cell Disease Association of America
231 East Baltimore Street Suite
800
Baltimore, MD 21202
410.528.1555
scdaa@sicklecelldisease.org
http://www.sicklecelldisease.org

Sickle Cell Association of Virginia
Principal contact: Minni Powell
14506 Hockliffe Loop
Midlothian, VA 23112
minni.powell@gmail.com
804-743-0807
https://www.vpap.org/lobbying/client/370502-sickle-cell-association-of-virginia/

The Heart of Gold Sickle Cell Foundation of Virginia, Inc.
P.O. Box 23681 Alexandria, VA 22304
Phone: 703-370-3234
https://heartogold.org/

Sickle Cell Association of the National Capital Area, Inc / SCANCA. Inc
P.O. Box 41479
Washington, DC 20018-08792
(202) 271-5733
email@scancainc.org
http://scancainc.org/

Sickle Cell Transplant Advocacy & Research Alliance/STAR
PO Box 96
Great Barrington, MA 01230
https://curesicklenow.org/