

# Hemoglobinopathies

## **Outcome without screening**

Individuals affected with sickle cell disease have lifelong hemolytic anemia with acute and chronic tissue damage secondary to the blockage of blood flow produced by the abnormally shaped red cells. Additional clinical manifestations include episodic vaso-occlusive crises, functional asplenia, sepsis, infections, splenic sequestration, and bone marrow aplasia. Sickle cell disease can be lethal, especially in early infancy or childhood because of overwhelming sepsis or splenic sequestration. Current United States predictions indicate an 85% chance that infants with homozygous sickle cell disease (SS) will survive to at least 20 years of age. However, complications include cerebrovascular accidents, neurologic deficits, aseptic necrosis of bones, leg ulcers, serious infections, renal concentrating defects, neoproliferative retinopathy, and delayed growth and sexual maturation.

The thalassemia syndromes are characterized by absent or deficient synthesis of one or more of the normal globin chains. This contrasts with the other hemoglobinopathies in which the variant hemoglobins are qualitatively or structurally abnormal. The major causes of mortality are iron overload and overwhelming infections following splenectomy. Iron overload is frequently due to excessive iron deposition as a result of blood transfusions and increased gastrointestinal absorption. Excess iron deposited in the heart, pancreas, liver, and other organs damages tissue and leads to cardiac failure, arrhythmias, diabetes mellitus, and liver failure. Beta thalassemia trait generally is not detected in the newborn period, but anemia becomes evident in the first 1-2 years of life. Because it is associated with mild anemia and small red blood cell size, it is often mistakenly identified as iron deficiency anemia. Homozygous thalassemia (thalassemia major) is a life-threatening condition that requires chronic transfusion and eventually iron chelation therapy to allow patients to lead a normal life. Clinically significant alpha thalassemia conditions can be responsible for fatal hydrops fetalis at birth. Other conditions, which may be detected in the newborn screening for hemoglobinopathies is Hemoglobin E thalassemia, a condition associated with chronic anemia, which is sometimes severe enough to require chronic transfusion and/or splenectomy, and Hemoglobin H disease, a lifelong chronic anemia.

## Incidence

Hemoglobinopathies are among the most common genetic conditions in the world. An average of 75 newborns each year are diagnosed through the newborn screening program in Louisiana each year. The following chart depicts recent findings resulting from newborn screening in Louisiana:

Figure. 1 Frequency of Hemoglobinopathy Phenotypes  
Louisiana 1995-2000\*\*

C disease (C, CF, FC)	8.49%
SC disease (CS, CSF, FCS, FSC, SC, SCF)	29.96%
S disease (FS, FSA <sub>2</sub> , S, SF, SFA <sub>2</sub> , SS)	56.90%
Sickle beta (+) thalassemia (FSA, SA, SAF, SFA, SFAA <sub>2</sub> )	4.03%
E disease (EE, FE)	0.42%
Unknown	1.49%

\*\*equals >100% due to rounding

## Outcome with screening

With screening, penicillin prophylaxis, and heightened vigilance, early death and morbidity from overwhelming sepsis can be significantly decreased. Death from acute splenic sequestration and aplastic crisis may be prevented or reduced. Risks of disability are lowered by aggressive treatment of infection, dehydration, and cerebral thromboses. Long-term clinical outcomes of patients identified by newborn screening programs are as yet undefined.

## Causes of hemoglobinopathies

Hemoglobinopathies are inherited disorders. In persons with the conditions in which the red blood cells (erythrocytes) become sickle shaped under certain circumstances, the hemoglobinopathies are termed "sickle cell diseases." This sickle shape of red blood cells reduces greatly the capability of the erythrocytes to function and causes illness in the affected person. The most prevalent condition is also known as Hemoglobin SS Disease, Sickle Cell Disease, Meniscocytosis and Drapanocytosis. Additionally the type of hemoglobin responsible for causing the sickling of erythrocytes may be found in persons who have thalassemia or variants of thalassemia, and in persons with other abnormal types of hemoglobins, such as Hemoglobin C.

The presence of diseases caused by abnormal hemoglobins are found in all racial and ethnic groups; Hemoglobin SS Disease is most commonly found in African Americans, but also occurs in persons of other races. The thalassemia group of diseases may be found most commonly among people whose ancestry is from the Mediterranean area as well as from Southeast Asia. It also occurs in African Americans.

### **Screening test and confirmation**

Screening for the hemoglobinopathies and thalassemias is done on filter paper dried blood spots from a heelstick, as are the other tests in the newborn screening program.

### **Treatment**

The primary rationale for newborn screening for these diseases stems from the high morbidity and mortality associated with overwhelming blood stream infection due to pneumococcal infection and the ability to prevent at least some of that problem. This results from early compromise of spleen function due to sickling of the erythrocytes in the spleen. Prior to the mid-1980s this was the leading cause of death in children with sickle cell disease. A national study found that the use of penicillin prophylaxis was highly effective in preventing infection. Therefore, it is important to diagnose sickle cell disease shortly after birth, so that penicillin prevention can be started.

When sickle cell disease is suspected on newborn screening, an extremely high priority is placed on contacting the family so that their child can start on prophylactic penicillin and an education program is initiated regarding the disease, its pattern of inheritance and genetic counseling for the family.

Discussion also includes other significant complications of sickle cell disease that can occur early in life, including pneumonia, anemia, enlargement of the spleen, swelling of the hands and feet, infection of the bone, and pain crises affecting various parts of the body.

Immunization with pneumococcal vaccine, in addition to all other routine immunizations of childhood is important, as it is for all children. Parent and patient education regarding rapid access to appropriate medical care for aggressive pain management, prompt recognition and early treatment of infections, management of dehydration and acidosis, blood transfusion therapy for selected problems (e.g., anemia and cerebrovascular events), and judicious use of oxygen reduce morbidity and mortality.

## **Special concerns and issues**

Of special concern is the marked clinical variability of sickle cell diseases ranging from mild symptoms to more severe symptoms to even death in early life. Clinical severity is influenced by the type of sickle cell disease present, e.g. SC disease is usually milder than SS disease. It is very important to differentiate sickle cell trait from sickle cell disease because the trait is rarely associated with any symptoms and does not lead to shortening of life, whereas sickle cell disease is invariably associated with clinical problems and does usually lead to a significant decrease in the life span.

## **Health Care Supervision**

A child who has sickle cell disease will need early and continuous health supervision. A local primary care physician is needed to provide routine preventive and acute care management. A pediatric hematology specialist is needed to advise, monitor and give intense counseling regarding the disease. Referral to a pediatric hematologist should be made as soon as a preliminary diagnosis is established. Contact the Genetic Diseases Program if assistance is required (504-219-4413).

A patient with sickle cell disease (SS, SC, S-Thalassemia) should be started on penicillin prophylaxis by 1½ to 2 months of age. If preliminary testing suggests sickle cell disease, penicillin should be instituted before 2 months of age. With the present laboratory methodology, it is not necessary to confirm sickle cell results with a repeat filter paper specimen.

In addition to the usual symptoms of anemia, such as fatigue and pallor, Sickle Cell Anemia is characterized by several types of life-threatening emergency conditions. Primary care providers and their medical staff working with sickle cell patients must be knowledgeable of these possible conditions and be prepared to assist the family in getting services as quickly as possible.

## **Possible complications**

### **Vaso-Occlusive Pain Episodes**

Occlusion of the small blood vessels due to sludging action of the abnormally-shaped erythrocytes occurs, causing varied symptomology. Severe abdominal pain or pain in other parts of the body may be experienced, so it is sometimes called the pain crisis. It may be precipitated by infection. In infants it is commonly manifest by swelling of hands and feet (hand-foot syndrome) caused by vaso-occlusion in these parts of the body. Occlusion of blood vessels in the brain may result in a stroke syndrome, with resultant hemiplegia or death.

### **Hyper-hemolytic Episode**

Massive destruction of red cells may occur, resulting in inadequate ability of the blood to carry oxygen to the vital organs of the body. Destruction of vital organ tissue results, which can lead to death.

### **Splenic Sequestration**

For unknown reasons, large amounts of blood may suddenly pool in the liver and spleen. Signs of shock or circulatory collapse develop rapidly, and death may occur. If the patient is supported by hydration and by blood transfusion, the sequestered blood may be remobilized.

### **Aplastic Episode**

Transient episodes occur when the bone marrow fails to produce erythrocytes. Profound and life-threatening anemia may then develop quickly. Aplastic crises are usually associated with infection. They are a serious, life-threatening complication.

### **Infections**

Children with Sickle Cell Disease are susceptible to severe, life-threatening infections, which are a major cause of morbidity and mortality.

### **Other Complications**

Because of chronic illness and anemia, the child with Sickle Cell Anemia may have growth retardation. He or she may develop impairment of liver function with resultant jaundice early in life. Gallstones have also been found to develop in the very young, as may renal, pulmonary and heart disease.

## Recommendations for Parents and Care Givers on Signs and Symptoms of Sickle Cell Disease Requiring Medical Care

The following is recommended counseling that should be given to parents and care givers on possible signs and symptoms of sickle cell disease that requires quick medical care. (All of this information is contained in the brochures “Sickle Cell Anemia (Hemoglobin SS Disease)” and “ Hemoglobin SC Diseases” (Appendix).

### **Fever**

If your baby feels warm, you should take the temperature. If the temperature is 100°, you should **immediately** call the physician or nurse. If the temperature is 101° or above, take the baby to your doctor or emergency room **immediately** for treatment. This may require that your baby be hospitalized and placed on intravenous antibiotics. Fever in babies with sickle cell anemia may indicate very serious, life-threatening infections.

### **Splenic Sequestration**

As blood is filtered through the spleen, sickled cells may be trapped and keep the blood from moving out of the spleen. Symptoms of this are swollen stomach, unusual sleepiness or irritability (fretfulness). **This is a serious life threatening problem. Go to an emergency room immediately. Have them call your baby’s doctor.** Your doctor or nurse can show you how to recognize this problem during your regular clinic appointment.

### **Swollen Hands and Feet**

One of the first symptoms of sickle cell anemia in babies may be swollen hands and feet. The hands and feet feel warm and sensitive to the touch. Contact your doctor for instructions on how to make your baby comfortable. This is NOT an emergency.

### **Anemia**

Because sickle cells do not live as long as the usual cells, your baby will be anemic, that is, your baby will have a low blood count. This is nothing usually to be concerned about; the baby’s body will adjust to this lower blood level. However, the baby may have less energy than other babies. If the baby appears listless, **contact the doctor immediately**, as this may indicate a suddenly more severe worsening of the anemia.

### **Jaundice**

When cells are destroyed they produce products in the blood that are carried off in waste. Sickle cells are destroyed at a much faster rate than regular red blood cells. Thus more of these blood break-down products are in the blood stream. These products can cause jaundice, giving a yellowish tint to the white of the eyes or an orange tint to the skin. **Please call your baby's doctor**, if this yellowish tint becomes more pronounced than usual.

### **Strokes**

In a small number of patients with sickle cell disease strokes can occur. These strokes can happen to children as young as 10 months of age. Any unusual drooling, weakness or muscles in the face (twisted or hanging mouth), inability to move arms or legs, dragging of the legs could be signs of stroke. **Go to an emergency room immediately. Have them call your baby's doctor.**

### **Skin Problems**

Breaks in the skin or untreated insect bites can sometimes lead to serious problems in patients with sickle cell disease. Sores, cuts, and insect bites should be cleaned and treated with a mild antiseptic. If the area is not healing or begins to get swollen or reddish, **contact the baby's doctor or nurse.**

## Calling the Physician

It is important to establish a relationship with your doctor and nurse, so that you get to know and trust each other. This relationship will make it easier for the doctor to take care of your baby, whether in the home or hospital.

*When calling the doctor, he or she will need to know:*

1. If there is a fever and how high? You **must** keep a thermometer on hand and learn how to read it so that you can give your doctor the exact temperature readings. This is very important for your baby's health.
2. Have you given your baby any medication? If so, what kind, how much, and when was the last dose given.
3. Is the baby eating and/or drinking fluids? It is very important that people with sickle cell anemia drink lots of fluids. You should pay close attention to the amount of fluid intake. If your baby is not drinking fluids, please let the doctor or nurse know.
4. Is the baby vomiting?
5. Is there pain—if so, where? Have you given your baby any pain medication? If so, how much, what kind, and when was the last dosage.
6. Does your baby have any of the symptoms listed previously?



## Regional Facilities Providing Specialized Sickle Cell Care

Region	Clinic Address	<i><b>Clinic Staff</b></i>
Region I	<b>Sickle Cell Center of Southern Louisiana</b> 1415 Tulane Avenue New Orleans, LA 70112 (504) 988-7386	Charles Scher, MD Marta Rozans, MD Charles Hempenway, MD Marshall Schorin, MD Mae Jones, RN
	<b>Children's Hospital</b> 200 Henry Clay Avenue New Orleans, LA 70118 (504) 896-9740	Raj Warriar, MD Maria Velez, MD Sherry Troquille, RN
	<b>Ochsner Foundation Hospital</b> 1516 Jefferson Highway Jefferson, LA 70121 (504) 842-5230	Rafael Ducos, MD Marquis Hodes, MD Patricia Shearer, MD Terese Sahuque, RN Michelle DeFrisco RN
Region II	<b>Earl K. Long Sickle Cell Clinic</b> 1401 North Foster Drive Baton Rouge, LA 70806 (225) 987-9061	Maria Velez, MD Raj Warriar, MD Sheila Moore, MD Tricia Esneault, RN
	<b>St. Jude Affiliate Clinic</b> 7777 Hennessy Boulevard - Suite 312 Baton Rouge, LA 70808 (225) 763-6337	Sheila Moore, MD Jeffrey Deyo, MD Kimberly Braud, RN
Region III	<b>Sickle Cell Center of Southern Louisiana</b> 1415 Tulane Avenue New Orleans, LA 70112 (504) 988-7386	Charles Scher, MD Marta Rozans, MD Charles Hempenway, MD Marshall Schorin, MD Mae Jones, RN
	<b>Leonard J. Chabert Medical Center</b> 1978 Industrial Boulevard Houma, LA 70363 (985) 873-1730	Rafael Ducos, MD Marquis Hodes, MD Patricia Shearer, MD
Region IV	<b>University Medical Center</b> 2930 Congress Street Lafayette, LA 70502 (337) 261-6179	Richard Howes, MD Stephen Barnes, MD Tammy Villalobes, RN
	<b>Women's &amp; Children's</b> 4600 Ambassador Caffery Parkway Lafayette, LA 70508 (337) 521-9250	Charles Scher, MD Marshall Schorin, MD Collette Rigsby

## Regional Facilities Providing Specialized Sickle Cell Care, continued

Region V	<b>W. O. Moss Regional Hospital</b> 1000 Walters Street Lake Charles, LA 70607 (337) 475-8420	Raj Warriar, MD Monta Lea Grimes, RN Debbie Potts
Region VI	<b>Alexandria Sickle Cell Clinic</b> Rapides Parish Health Unit 1200 Texas Avenue Alexandria, LA 71301 (318) 487-5282	Majed Jeroudi, MD Louise Karisny, RN Barbara Costantino, RN
Region VII	<b>Sickle Cell Center of Northern Louisiana</b> LSU Medical Center 1501 Kings Highway, Room 5304 (318) 813-1100	Majed Jeroudi, MD Nerissa Goodman-Sessions, RN
Region VIII	<b>Monroe Sickle Cell Center</b> 1650 Desiard St  Monroe, LA 71211 (318) 361-7282	Majed Jeroudi, MD Melissa Brown, RN
Region IX	<b>Sickle Cell Center of Southern Louisiana</b> 1415 Tulane Avenue New Orleans, LA 70112 (504) 988-7386	Charles Scher, MD Marta Rozans, MD Charles Hempenway, MD Marshall Schorin, MD Mae Jones, RN

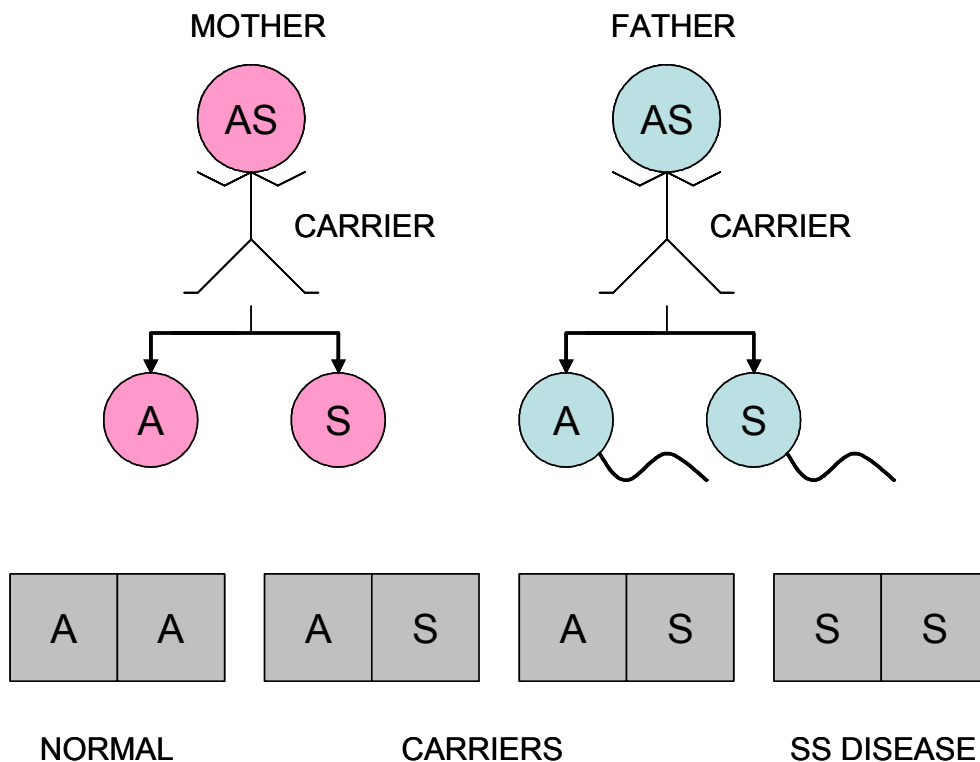
## Counseling Regarding Sickle Cell Trait and Disease

Both trait and disease require counseling. Counseling may be provided by the PCP, the Regional Sickle Cell Foundation, public health nurses or Genetic Diseases Consultant. Explain to the person what the results mean in terms of medical care and life style. For example, if the results show sickle cell disease, discuss need for regular medical care. If the person has sickle cell trait, discuss in terms of lack of medical problems, but the risk involved because of heritable nature of the disorder when mating with another carrier of sickle cell trait or of another hemoglobinopathy. The primary aim of counseling is to make people aware that they are carriers of sickle cell hemoglobin so they can make an informed decision about having children. The risks are explained below.

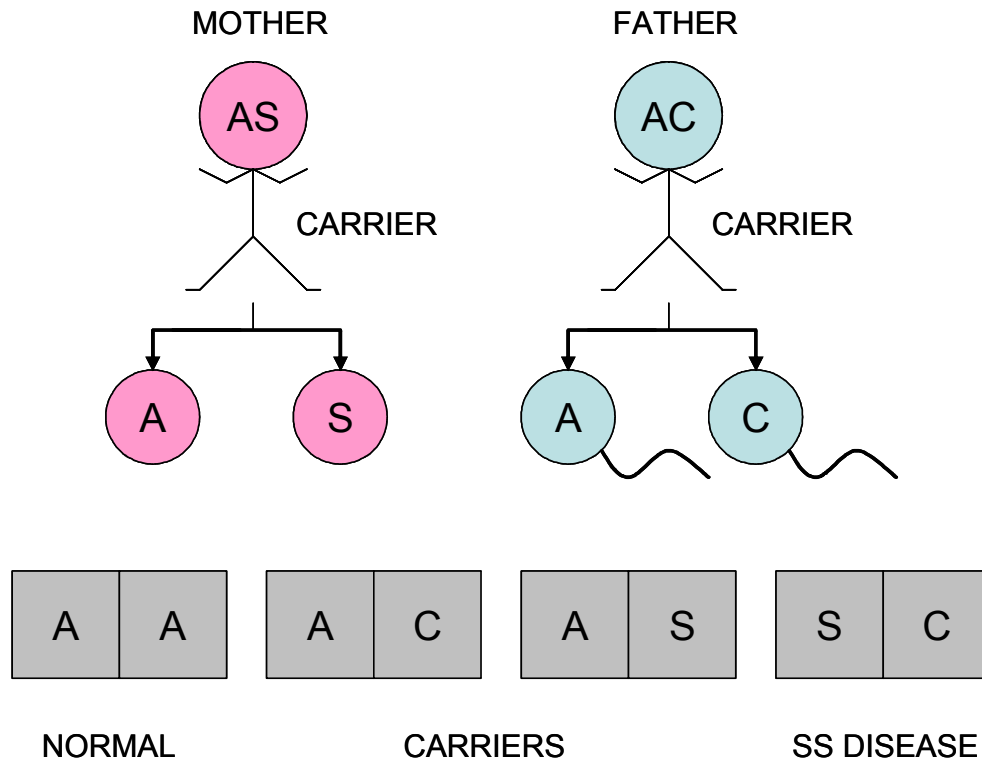
Several pamphlets are available from the Genetic Diseases Program: ("Sickle Cell Anemia", "Sickle Cell Carrier (Trait)", "Hemoglobin SC Disease.") A copy of the appropriate pamphlet should be used during counseling of those with trait or disease.

Sickle Cell Anemia (Hemoglobin SS Disease) is transmitted through carriers, and we are able to identify the carrier state through hemoglobin electrophoresis. Abnormal genes must be carried by both parents to have a child with sickle cell disease. The following counseling notes how parents pass on sickle cell trait or anemia. These charts illustrate the Mendelian recessive pattern of inheritance, and the diagrams can be used to illustrate the probabilities in the following patterns:

### SS Disease



## SC Disease



1. If one parent has normal hemoglobin (AA) and the other is a carrier having sickle cell trait (AS), their childrens' hemoglobin will be as follows:
  - 50% trait
  - 50% normal
  - none will have the disease
2. If one parent has normal hemoglobin and the other has hemoglobin SS disease, their childrens' hemoglobin will be as follows:
  - 100% trait
  - none will have the disease
3. If each parent has sickle cell trait, their childrens' hemoglobin will be as follows:
  - 25% normal
  - 50% sickle cell trait
  - 25% sickle cell anemia

4. If both parents have sickle cell anemia:
  - All of their children will have sickle cell anemia
5. If one parent has sickle cell anemia and the other has sickle cell trait, their children's hemoglobin will be as follows:
  - 50% trait
  - 50% sickle cell anemia

NOTE: Hemoglobin S is used here as an example. The same pattern of Inheritance applies to other abnormal hemoglobins and with mixtures, such as hemoglobin SC disease or sickle thalassemia.

Sickle cell disease counseling should also include the following:

- Attendance at Sickle Cell Centers or evaluation and monitoring by a pediatric hematologist.
- Source of Medical Home
  - Preventive services (regular check-ups, immunizations, etc)
  - Illness care
- Expected place for hospitalizations
- Insurance availability of Medicaid eligibility
- Usual local source of care
- Referral to Sickle Cell Anemia Foundations

## Patient Assistance

Louisiana Association for Sickle Cell Anemia (LASCA) has regional Chapters which give counseling and may offer assistance for patients with Sickle Cell Disease to cover cost of one or more services: medication, transportation, and emergency services, as needed. Local health unit personnel should contact the nearest Chapter and see what services are available.

### Sickle Cell Foundation Offices and Contact Persons

Foundation	Address	Phone Number
Baton Rouge Sickle Cell Anemia Foundation	2301 North Blvd Baton Rouge , La. 70806	225-346-8434
Acadiana Sickle Cell Anemia Foundation	612 Surrey St. Lafayette, La. 70501	337-234-1541
LSU / W.O. Moss Regional Medical Center	1000 Walters St. Lake Charles, La. 70805	337-475-8828
Sickle Cell Anemia Research Foundation	2625 Third St. Alexandria, La. 71309	318-487-8019
Sickle Cell Disease Association of America	3658 Judson St. Shreveport, La. 71109	318-636-5300
Northeast Sickle Cell Anemia Foundation	1604 Winnsboro Road Monroe, La. 71202	318-322-0896