

# **SICKLE CELL DISEASE AND OTHER HEMOGLOBINOPATHIES**

## **Definition**

Sickle cell diseases comprise a group of genetic disorders characterized by the presence of hemoglobin S (Hb S). Hb S can cause red blood cells to change from their usual biconcave disc shape to a crescent or sickle shape during deoxygenation. The red blood cell resumes a normal configuration, but after repeated cycles of “sickling and unsickling,” the red blood cell becomes damaged permanently, and hemolysis occurs. This hemolysis is responsible for the anemia that is the hallmark of sickle cell disease.

## **Incidence**

Sickle cell disease affects 1 in 375 African-Americans and more than 1 in 50,000 Americans. It is estimated that 8% of the African American population carries the sickle cell trait. The disease can also affect those of Mediterranean, Caribbean, South and Central American, Arabian, or East Indian ancestry.

## **Inheritance**

Sickle hemoglobin (Hb S) is inherited as autosomal recessive from both parents or Hb S from one parent and a gene for an abnormal hemoglobin or beta-thalassemia from the other parent.

## **Characteristics**

Acute and chronic tissue injury can occur when blood flow through the vessels is obstructed by abnormally shaped red cells. Complications include painful episodes involving soft tissues and bones, acute chest syndrome, priapism, cerebral vascular accidents, and both splenic and renal dysfunction. Common causes of mortality among children with sickle cell disease include bacterial infections, splenic sequestration crisis, and acute chest syndrome.

## **Variant Forms**

Types of sickle cell disease include sickle cell anemia (SS), hemoglobin SC disease, sickle beta thalassemia, and SE disease. Other hemoglobin diseases include hemoglobin CC and EE diseases.

## **Newborn Screening Methodology**

The laboratory method used is Isoelectric Focusing (IEF) and High Performance Liquid Chromatography (HPLC).

## **Confirmation**

Health care providers should seek consultation from a Pediatric Hematology Consultant, (319) 356-1400. If the newborn screen result is abnormal, a second specimen should be obtained and sent to the INMSP lab. DNA analysis of the infant’s beta globin gene complex also may be used to establish a definitive diagnosis.

## Treatment and Outcome

Any sign of illness in an infant with sickle cell disease is a potential medical emergency. Infants with sickle cell disease should receive standard well baby care, including pneumococcal vaccination. Infants with documented or suspected sickle cell anemia or Hb S/ Beta thalassemia should be started on twice-daily oral prophylactic penicillin as soon

as possible, but no later than two months of age. Infants with suspected sickle cell disease should be maintained on prophylactic penicillin until the definitive diagnosis is established. Parents of infants with sickle cell disease should be instructed in all aspects of routine childcare and should be able to determine accurately the infant's temperature. Parents must understand the importance of prompt assessment of the infant by a physician knowledgeable about sickle cell disease when there is fever, pallor, unexplained irritability, diarrhea, vomiting, or other signs of illness. Some infants will be identified as a hemoglobin trait carrier. Practitioners are strongly encouraged to have blood specimens drawn on each parent to determine their carrier status. Genetic counseling should be offered. The Regional Genetics Consultation Service (1-800-260-2065) provides genetic counseling and evaluation at outreach clinics statewide.

## Screening Practice Considerations

- The newborn screen should detect most abnormal hemoglobin subtypes. However, it is not always possible to identify beta thalassemia with this test.
- The newborn screen for hemoglobinopathies is not affected by age at collection.
- Blood transfusions may result in false negative results. **Always obtain a newborn screening specimen prior to a transfusion.**
- The primary purpose of hemoglobinopathy screening is the identification of infants with sickle cell diseases for whom early intervention has been shown to markedly reduce morbidity and mortality.
- The screening test is not diagnostic and all abnormal results should be confirmed.
- Only **filter paper** specimens are tested in the INMSP. All initial abnormal hemoglobin results should be immediately followed up with a second filter paper newborn screening specimen.
- Solubility testing (sickle prep or sickle dex) should never be used. It is an inadequate method of screening.
- A properly performed hemoglobin electrophoresis should be used to verify the presence/absence of an abnormal hemoglobin.
- Hemoglobinopathies are complex disorders, and practitioners will be sent consult follow-up resources for more information concerning abnormal screening results and appropriate follow-up and treatment.

## Explanation of Report Results/Comments Specific to Hemoglobinopathies

### Normal expected patterns:

FA	Fetal hemoglobin is greater than adult hemoglobin. Normal pattern in newborn < 3 weeks of age.
AF	Adult hemoglobin is greater than fetal hemoglobin. Normal pattern in newborn >3 weeks of age, provided NO TRANSFUSION had taken place within the last eight weeks and anemia is not suspected.

**Transfused/unknown transfusion status:**

Blood transfusions will interfere with the interpretation of screening results. If patient was transfused, resubmit another **filter paper** specimen eight weeks after the last transfusion.

A>F	Adult hemoglobin is greater than or equal to fetal hemoglobin. IF TRANSFUSED, send other FILTER PAPER specimen collected at least 8 weeks after the last transfusion.
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**F only:**

Individuals with only fetal (F) hemoglobin without detectable normal hemoglobin A (adult) need immediate follow-up testing to determine if this is caused by prematurity or the absence of the hemoglobin A (adult) gene.

FF	Hemoglobin F only may indicate a delayed appearance of hemoglobin A (prematurity), hereditary persistence of fetal hemoglobin, or betathalassemia major.
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**Disease:**

Individuals with disease have two abnormal hemoglobin genes (i.e., SS, SC, CC, etc.) without the normal hemoglobin gene A (adult). This clinically significant condition needs immediate followup. Practitioners should contact a Hemoglobinopathy Program Consultant at (319) 356-1400 regarding follow-up testing and treatment.

CC	Homozygous hemoglobin CC.
EE	Homozygous hemoglobin EE.
EE + Bart's	Homozygous hemoglobin EE with possible alpha-thalassemia.
S-Beta-Thalassemia	Heterozygous hemoglobin S and beta-thalassemia.
SC	Heterozygous hemoglobins S and C.
SS	Homozygous hemoglobin SS.
SS + Bart's	Homozygous hemoglobin SS, with possible alpha-thalassemia.
VV	Homozygous hemoglobin unknown variant which may or may not be clinically significant.

**Trait:**

Individuals with trait have a normal hemoglobin gene, A (adult) and an abnormal hemoglobin gene (i.e., S, C, E, etc.). This heterozygous condition is usually clinically insignificant. Genetic counseling is recommended for all individuals identified as carriers.

AS	Heterozygous sickle cell trait.
AC	Heterozygous hemoglobin C trait.
AV	Heterozygous unknown trait that may or may not be clinically significant.
AE	Heterozygous hemoglobin E trait.

AD	Heterozygous hemoglobin D trait.
FA + Bart's	This pattern MAY indicate some forms of alpha-thalassemia.
AS + Bart's	Heterozygous sickle cell trait and possible alpha-thalassemia.

**About Thalassemias:**

Bart's hemoglobin appears in the first few weeks of life but thereafter cannot be demonstrated on electrophoresis. The presence of Bart's hemoglobin is associated with alpha thalassemia, but INMSP testing cannot distinguish between alpha-thal-2 homozygous and alpha-thal-1 heterozygous conditions (present with mild anemias). Alpha-thal-2 heterozygous (silent carrier) conditions may go undetected. *Note: Beta thalassemia trait cannot always be detected on newborn screening samples.*

FA + Bart's	This pattern MAY indicate alpha-thalassemia.
AS + Bart's	Sickle cell trait with possible alpha-thalassemia.
AE + Bart's	Hemoglobin E trait with possible alpha-thalassemia.

**Other Sites of Reference**

Sickle Cell Anemia and Stroke

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/scstroke.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/scstroke.htm)

Chest Syndrome With Sickle Cell Disease

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/chest.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/chest.htm)

Pneumococcal Infection and Penicillin Sickle Cell - WA State Dept. of Health

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/pneumo.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/pneumo.htm)

NORD - Sickle Cell

Website: [www.rarediseases.org/search/rdbdetail\\_abstract.html?disname=Sickle%20Cell%20Disease](http://www.rarediseases.org/search/rdbdetail_abstract.html?disname=Sickle%20Cell%20Disease)

March of Dimes - SCD

Website: [www.marchofdimes.com/aboutus/681\\_1221.asp](http://www.marchofdimes.com/aboutus/681_1221.asp)

Sickle Cell Information Center

Website: [www.emory.edu/PEDS/SICKLE/index.htm](http://www.emory.edu/PEDS/SICKLE/index.htm)

Harvard Medical School - Joint Center for Sickle Cell and Thalassemic Disorders

Website: [www-rics.bwh.harvard.edu/sickle/](http://www-rics.bwh.harvard.edu/sickle/)

OMIM - Sickle Cell

Website: [www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?603903](http://www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?603903)

Sickle Cell Disease Association of America, Inc.

Website: [www.sicklecelldisease.org/](http://www.sicklecelldisease.org/)

PAIN in the child with Sickle Cell Disease

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/Pain.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/Pain.htm)

The Infant and Young child with Sickle Cell Anemia

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/chwsick.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/chwsick.htm)

Sickle Cell Anemia: A Parent's Guide for the School Age Child

Website: [www.doh.wa.gov/EHSPHL/PHL/Newborn/scpg.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/scpg.htm)

MUMS - National Parent-to-Parent Network

Website: [www.netnet.net/mums/](http://www.netnet.net/mums/)

### **Support Groups**

Sickle Cell Foundation of Georgia

[www.sicklecellatlaga.org/](http://www.sicklecellatlaga.org/)

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