Hemoglobinopathies

A hemoglobinopathy (hemoglobin disorder) is a condition that affects the red blood cells and originates from genetically determined changes in the molecular structure of hemoglobin.

In the clinical laboratory, the hemoglobin Isoelectric Focusing (IEF) and High-Performance Liquid Chromatography (HPLC) tests will reveal multiple hemoglobin disorders with varying degrees of severity.

The effects range from mild anemia in Hemoglobin C disease (Hemoglobin CC) and C, Beta (β) Thalassemia, to severe pain episodes, growth delays, increased susceptibility to infections, and persistent anemia in Sickle Cell Anemia (Hemoglobin SS) and S, β Thalassemia.

Hemoglobinopathies are inherited in an autosomal recessive pattern. Carriers of a single abnormal gene for one of these disorders are considered to have a trait. Persons with a trait will have red blood cells that contain a mixture of normal and abnormal hemoglobin. Most hemoglobin traits cause no disease or anemia under normal physiologic conditions* (see FAB and *Special Considerations* below).

Inheritance:	Autosomal recessive
Estimated Incidence:	1:400 African Americans (sickling disorders) 1:2500 All Races & Ethnicities (sickling disorders)
Neonatal Presentation:	None
Method of Notification:	All abnormal results are called and faxed to the provider of record.
Next Steps if Abnormal:	**Sickling disorders - Refer to a pediatric hematologist** if the hemoglobin pattern is FS, FSA, FSB, FSC, FSD, FSE, FSG, FSO or FSV. **Report all subsequent findings to the SC Newborn Screening program.** **Non-sickling disorders and Thalassemia - Refer to a pediatric hematologist. Report all subsequent findings to the SC Newborn Screening program.** If all other newborn screening results are normal, **a repeat newborn screening specimen is not required**. The initial sample will be sent to a reference lab for hemoglobin confirmation. All hemoglobinopathies and traits - Refer family to a sickle cell foundation for family testing, education, and genetic counseling.

Screening Results:

The following table outlines the most common results of the newborn hemoglobin screen. It is important to remember that PREMATURITY AND TRANSFUSIONS AFFECT TEST RESULTS. Each type of hemoglobin in the infant's blood is identified by a letter on the test result (e.g. F=Fetal, A=Adult or normal, S=Sickle, V=other unknown variant).

The position of the letter represents the amount of hemoglobin type present with the hemoglobin of greatest concentration listed first. (Example: "FSA" usually indicates a sickling disorder and "FAS" indicates a trait).

When hemoglobin disorder is suspected, specific instructions will be sent from the program. A portion of the abnormal bloodspot will also be sent to the Children's Hospital of Oakland Research Institute (CHORI) for confirmatory testing. **If all other newborn screening results are normal, a repeat specimen is not required.**

Newborn's Hemoglobin Result	**Potentially indicative of:**	**Sent to CHORI?**
FA	Normal Newborn Hemoglobin	NA
AF	Normal or transfused hemoglobin	NA
FS	Sickle Cell disease, Sickle β0-thalassemia, or Sickle with Hereditary Persistence of Fetal Hemoglobin (S-HPFH)	Yes
FSA	Sickle β+-thalassemia or Sickle cell trait	Yes
FSB (FS + Bart's)	α Thalassemia with Sickle Hemoglobin	Yes
FSC	Sickle C disease, SC Harlem	Yes
FSD	Sickle D Disease	Yes
FSE	Hemoglobin SE Disease	Yes
FSG	Sickle Cell Anemia, Sickle cell β Thalassemia, Sickle G Philadelphia	Yes
FSO	Sickle O Arab Disease	Yes
FSV	Sickle with Variant Hemoglobin pattern	Yes
FC	Homozygous Hemoglobin C disease or Hemoglobin C β0 thalassemia	Yes
FCA	Hemoglobin C β+ thalassemia or Hemoglobin C trait	Yes
FCE	Hemoglobin CE Disease	Yes
FCV	Hemoglobin C Variant	Yes
FDD	Homozygous Hemoglobin D, Hemoglobin D Thalassemia	No
FDA	Hemoglobin D/β Thalassemia or Hemoglobin D trait	No
FDV	Hemoglobin D Disease, Hemoglobin D Thalassemia, or Hemoglobin D trait	No

FE	Homozygous Hemoglobin E Disease, Hemoglobin E β+ thalassemia, or Hemoglobin E β0 thalassemia	Yes
FEA	Hemoglobin E β+ thalassemia or Hemoglobin E trait	Yes
FEV	Hemoglobin E Disease, Hemoglobin E β+ thalassemia, Hemoglobin E β0 thalassemia, or Hemoglobin E trait	Yes
FV	Unknown hemoglobin variant	Yes
FO	Homozygous Hemoglobin O-Arab	No
FVA	Unknown hemoglobin variant	No
FOA	Hemoglobin O-Arab/β+ Thalassemia or Hemoglobin O-Arab/β0 Thalassemia	No
FF	Premature Infant, Hereditary Persistence of Fetal Hemoglobin (HPFH) or Homozygous β thalassemia major	Yes
*FAB >= 15% (Bart's)	Hemoglobin Bart's - α thalassemia of unknown severity to Hemoglobin H disease	Yes
FAB < 15% (Bart's), FAC, FAD, FAE, FAG, FAO, FAS, FAV, or FA + fast band	Various Hemoglobin traits/carriers	No

Please consult with a pediatric hematologist for further recommendations.

Treatment:

Sickling disorders – The National Institutes of Health (NIH) clinical guidelines suggest Penicillin/antibiotic prophylaxis beginning at 2 months of age and continuing through early childhood. Prompt evaluation and management of acute illness to lessen development of sickling crises, particularly if fever is present.

An alternative antibiotic is available for children who are allergic to penicillin therapy. Health care monitoring and maintenance with appropriate immunizations are imperative to the health of the baby, and pneumococcal conjugate vaccine immunizations also are recommended, beginning at 2 months of age.

Appropriate pain management strategies (such as use of extra fluids, oral analgesics, and comfort measures) including rapid triage if home management strategies are not sufficient.

Transfusion may be necessary in certain instances. Medications to increase the production of fetal hemoglobin and lower leukocyte counts such as hydroxyurea may be used in certain children.

A blood or marrow transplant is the only known cure for sickle cell disease (SCD). However, transplant has serious risks and is only used in patients with severe SCD who have symptoms

including stroke, acute chest syndrome, and frequent pain episodes. The transplant replaces diseased blood-forming cells with healthy ones.

The type of transplant used to treat SCD is an allogeneic transplant. This type of transplant uses healthy blood-forming cells from a family member, unrelated donor, or umbilical cord blood unit. For an allogeneic transplant, a patient gets chemotherapy (with or without radiation) prior to transplant to prepare his or her body for the treatment.

Then, the replacement cells are infused into the patient's blood stream. From there, the cells find their way into the bone marrow, where they start making healthy white blood cells, red blood cells and platelets. The entire process, from the start of chemotherapy or radiation until hospital discharge, can last weeks to months followed by many months of recovery at home.

Special Considerations

Transfusion - Transfusion of red blood cells prior to drawing the newborn screening specimen will affect the hemoglobin result. Repeat screening for hemoglobinopathies should be done 120 days after the last transfusion. If the date of the last transfusion is unknown, put the date of hospital discharge on the collection form next to "**Transfused**".

Specimen Analysis at the Reference Laboratory - The initial newborn screening bloodspots for infants with hemoglobin results indicative of disease are sent to the Children's Hospital of Oakland Research Institute (CHORI) for more specific hemoglobin analysis and genetic testing. The result of the CHORI analysis is sent to the provider of record upon receipt by the Public Health Laboratory.

Follow-up Assistance and Coordination of Care - DHEC Children and Youth with Special Healthcare Needs (CYSHCN) Sickle Cell Program assists primary care providers to ensure infants identified with a sickling disorder are seen by a pediatric hematologist within the first six weeks of age. They can help coordinate activities with pediatric hematologists, Sickle Cell Foundations, local health departments and hospitals, so that families are directed to the services closest to them.

In coordination with the CYSHCN Sickle Cell Program and the Sickle Cell Foundations of South Carolina, counseling, education, and other resources are offered to families of infants diagnosed with a hemoglobin disorder or trait identified through newborn screening.

The goals of education and counseling are to increase the understanding of genetic diseases, discuss disease management options, and explain the risks and benefits of family testing. Counseling sessions focus on giving vital, unbiased information and non-directive assistance in the family's decision-making processes.

****Participation in Sports or Extreme Physical Activity*** - Some persons with sickle cell trait (FAS or AS) may exhibit a sickling crisis associated with extreme physical activity. Precautions must be taken to lessen the chance for exertional rhabdomyolysis.

Sickle Cell Foundation Contacts in South Carolina

Community Based Organizations (CBO's) for support:

COBRA Human Services Agency Sickle Cell Program
3962 Rivers Ave
PO Box 71473
Charleston, SC 29415
Toll Free (800) 354-4704
(843) 225-4866, Service Line
(843) 225-4869, Fax
cobraagency@bellsouth.net

Orangeburg Area Sickle Cell Foundation
825 Summers Ave
PO Box 892
Orangeburg, SC 29116
(803) 534-1716, Phone
(803) 531-2422, Fax
orangeburgsickle@aol.com

James R. Clark Memorial Sickle Cell Foundation
1420 Gregg St
Columbia, SC 29201
Toll Free (800) 506-1273
(803) 765-9916, Phone
(803) 799-6471, Fax
www.jamesrclarksicklecell.org
office@jamesrclarksicklecell.org

Louvenia Barksdale Sickle Cell Anemia Foundation
645 S Church St
PO Box 191
Spartanburg, SC 29304
(864) 582-9420, Phone
(864) 582-9421, Fax
www.barksdalesicklecell.org
ldbarksdale@charter.net

Additional Resource

Centers for Disease Control and Prevention, Sickle Cell Disease (SCD) National Resource
https://www.cdc.gov/ncbddd/sicklecell/index.html