Kansas Department of Health and Environment

Hemoglobin Disorders (Hemoglobinopathies)
Information for Healthcare Professionals

Hemoglobin disorders include (1) structural hemoglobin variants (S, C or E), which cause sickle cell disease and (2) thalassemias, resulting from defective alpha and beta globin production. Both types of disorders seemingly developed as a form of carrier resistance against malaria and are widespread in areas profoundly affected by malaria, predominantly Africa, Southeast Asia, the Mediterranean, and the Middle East. A detailed family history can facilitate the diagnostic process.

✓ Clinical Symptoms

Clinical symptoms of hemoglobinopathies, depending on the genotype, range from mild to severe. Sickle cell anemia (Hb SS, accounting for about 60% of all sickle cell disease) is the most severe presentation, though it rarely presents in the newborn period due to postnatal persistence of fetal hemoglobin. The red blood cells distort because they contain an abnormal type of hemoglobin (hemoglobin S), instead of the normal hemoglobin (hemoglobin A). Sickled blood cells are destroyed by the body faster than normal blood cells, which can lead to the body receiving an inadequate supply of oxygen. Also, sickled blood cells can become trapped in blood vessels, reducing or blocking blood flow. This can damage organs, muscles, and bones and may lead to life-threatening conditions. Sickle cell disease is most commonly found in populations of African descent. It is also relatively common in people from Central and South America, Saudi Arabia, India, and the Mediterranean. Infants with Hb SS disease are at risk for:

- anemia
- bacterial infection and fever
- painful swelling of the hands and feet
- acute chest syndrome (coughing, breathing problems, pain)
- stroke
- splenomegaly
- aplastic crisis

Sickle cell disease (Hb SC or Hb SB-thal) generally will have a milder presentation, though most children with sickle cell disease will have some degree of anemia and are at risk of developing any of the above symptoms.

The thalassemias are classified according to the ineffectively synthesized globin chains. There are two major forms of thalassemia: alpha thalassemia (alpha chain deficiency) and beta thalassemia (beta chain deficiency). Alpha thalassemia is most common in people of Southeast Asian, Indian, Middle Eastern and African descent. Beta thalassemia is most common in people from the Mediterranean and the Middle East, but is also found in Africans and Southeast Asians. Beta thalassemia mutations are population specific: each ethnic group has its own subset of common mutations.

Only the most severe forms of thalassemia will have a neonatal presentation. Alpha thalassemia major (hydrops fetalis) is generally incompatible with life. Fetuses with alpha-thal major will develop severe anemia, fluid accumulation in the tissues, and heart failure. Most are stillborn or die shortly after birth. Beta thalassemia major (also called Cooley anemia) results in life-threatening anemia. Individuals with beta thalassemia major require regular blood transfusions and chelation therapy to reduce iron overload.

✓ Incidence

Sickle cell disease (Hb SS, SC, or SB) occurs in approximately 1 in 400 births in the African American population. Thalassemia is rare in the U.S., but recent immigration patterns suggest that thalassemia is of increasing concern.

✓ Genetics and inheritance of hemoglobinopathies

Mutations in the *HBB* gene (hemoglobin beta chain) cause sickle cell disease and beta thalassemia. Mutations in *HBA1* and *HBA2* lead to alpha thalassemia. All of these conditions are inherited in an autosomal recessive manner. Pregnancies between two carriers have a 25% chance of producing an affected child, a 50% chance of producing an unaffected carrier, and a 25% chance of producing an unaffected child who is not a carrier.

It is also important to be aware of compound heterozygous states, when children are born with two different forms of variant hemoglobin. Hemoglobin SC disease and Hemoglobin SB-thalassemia are examples of compound heterozygosity. In general, compound heterozygotes have less severe anemia than their homozygous counterparts, but will have more symptoms than those individuals who carry one normal gene.

✓ Treatment

Treatment for sickle cell disease is lifelong and should take place under the care of pediatric hematologists experienced with hemoglobin disorders. Prophylactic antibiotics are administered up to twice a day to prevent bacterial infection, and painful crises are managed with analgesia and hydration. It is important to keep immunizations current to prevent illness. Families should be trained to monitor and manage minor symptoms at home, and have a plan in place for times when medical attention becomes urgently needed.

Treatment for thalassemia (alpha and beta) may require occasional-to-regular blood transfusions, depending on the severity of symptoms, along with iron chelation therapy.

✓ Screening Methodology /Confirmation of Diagnosis

Primary newborn screening for hemoglobinopathies utilizes high performance liquid chromatography (HPLC) to determine the presence of variant hemoglobins. Follow-up evaluation of the newborn for symptoms and confirmatory testing by repeat HPLC or hemoglobin electrophoresis, CBC, parental testing and/or molecular DNA analysis should be performed as soon as possible. False positive and false negative results are possible in newborn screening. Specimens should be drawn before administration of medications or transfusions. False results can also occur if the specimen is mishandled or exposed to heat, or if screening is delayed.

✓ What to do After Receiving Presumptive Positive Abnormal Hemoglobin Results

1) **An abnormal Hb screen requires an immediate check on the clinical status of the baby.**
2) **Refer the infant to a pediatric hematologist, or to a dedicated sickle cell clinic.**
3) **Collection of a blood specimen for confirmatory testing.**
4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**

✓ Communication of Results to Parents

If a baby has a presumptive abnormal hemoglobin newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with a hemoglobin disorder, the following points should be conveyed to parents:

- ***Parents should understand that treatment is lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

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