ACMG
American College of Medical Genetics and Genomics
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ACT Sheet

Newborn Screening ACT Sheet

[Hemoglobin FS]

Hemoglobin S/S or Hemoglobin S/Beta Zero Thalassemia (Hb S/S or HbS/β^0 Thalassemia)

Differential Diagnosis: Homozygous Hemoglobin S; Hemoglobin S/Beta Zero (β^0) Thalassemia); Hemoglobin S/Beta Plus (β^+) Thalassemia; Hemoglobin S/Hereditary Persistence of Fetal Hemoglobin (HPFH).

Condition Description: Hemoglobin S/S and Hemoglobin S/β^0 Thalassemia are inherited red blood cell disorders characterized by abnormal hemoglobin production. They are due to genetic changes in the beta hemoglobin gene. Although asymptomatic at birth, symptoms begin as Hb F decreases and Hb S predominates. The clinical course is highly variable, ranging from asymptomatic to life-threatening infections, strokes, acute chest syndrome, end organ damage, and pain crises. Hb S/HPFH is clinically benign.

You Should Take the Following Actions:

- Inform the family of the newborn screening result.
- Ascertain clinical status (newborns are expected to be asymptomatic).
- Evaluate the newborn (assess for splenomegaly and send CBC).
- Administer prophylactic penicillin.
- Consult with sickle cell specialist immediately with in person follow up by no later than 12 weeks of age.
- Coordinate confirmatory diagnostic testing and management as recommended by specialist.
- Provide family with basic information about Hemoglobin S/S or Hemoglobin S/Beta Zero (β^0) Thalassemia including the need for urgent evaluation if fever of ≥ 38.5ºC (101ºF), or signs of stroke or splenic sequestration.
- Refer for genetic counseling.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: The hemoglobins are listed in order of the amount of hemoglobin present on the newborn screen (F>S). Isoelectric focusing, high performance liquid chromatography (HPLC) or capillary zone electrophoresis is used to confirm the newborn screening result. Complete blood count: the CBC, smear and reticulocyte count may be normal at birth but over the first months of life demonstrate a worsening anemia, with an increasing reticulocyte count and sickle cells on smear. Molecular genetic testing is required to distinguish Hb S/S, Hb S/β^0 Thalassemia, and Hb S/HPFH, and to characterize the specific Thalassemia variant present.

Clinical Considerations: Newborns with Hemoglobin S/S are generally asymptomatic. Hemolytic anemia and vaso- occlusive complications can develop during infancy or in early childhood. Without appropriate treatment, complications may include life-threatening infection, splenic sequestration, pneumonia, acute chest syndrome, pain episodes, aplastic crises, dactylitis, priapism, osteonecrosis, and stroke. Comprehensive care including family education, a modified immunization schedule, prophylactic penicillin, therapeutic interventions such as hydroxyurea, prompt treatment of acute vaso-occlusive events, and screening for early signs of organ damage reduces morbidity and mortality. Most newborns with HbS/β^0 Thalassemia have a clinical course similar to Hb S/S. Hb S/HPFH is typically benign. Solubility testing (Sickledex) should not be used to confirm the diagnosis. Iron supplements should be avoided unless iron deficiency is documented.

Referral (local, state, regional, and national):

Children's of Alabama
Pediatric Hematology
1600 7th Avenue South, ACC 512
Birmingham, AL 35233
Phone: (205) 638-2390

St. Jude's Clinic at Huntsville Hospital
Pediatric Hematology
910 Adams Street, Suite 310
Huntsville, AL 35801
Phone: (256) 265-5833 or 1-866-595-5449

University of South Alabama Sickle Cell Center
Pediatric Hematology
1504 Springhill Avenue, Suite 5230
Mobile, AL 36604
Phone: (251) 415-5172 or (251) 405-5147