ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

Newborn Screening ACT Sheet

[Hemoglobin F-Only; Hemoglobin F With Decreased A]

Transfusion Dependent Beta (β)-Thalassemia, Non-Transfusion Dependent Thalassemia, (β -Thalassemia Major; β -Thalassemia Intermedia)

Differential Diagnosis: Transfusion Dependent β Thalassemia, (β Thalassemia Major); Non transfusion Dependent Thalassemia, (β Thalassemia Intermedia); Hb β+ /β+ Thalassemia; Hb β0-Thalassemia; Hb β0/β+ Thalassemia; hereditary persistence of fetal hemoglobin (HPFH); prematurity.

Condition Description: The β Thalassemias often cannot be distinguished by newborn screening and following their clinical course is often required to accurately classify them. They are inherited red blood cell disorders characterized by abnormal hemoglobin production. The β Thalassemias are caused by the lack of β globin chains compared to α-globin chains resulting in an absence or deficiency of normal hemoglobins (HbA, and possibly HbA2 and HbF). Although asymptomatic at birth, individuals with these diagnoses develop a profound microcytic anemia and can require chronic or intermittent transfusions and chelation therapy.

You Should Take the Following Actions:

- Inform family of the screening result.
- Ascertain clinical status (newborns are expected to be asymptomatic).
- Consult with thalassemia specialist immediately with in person follow up no later than 12 weeks of age.
- Evaluate the newborn (newborns are expected to be asymptomatic).
- Coordinate confirmatory diagnostic testing and management as recommended by a thalassemia specialist.
- Provide family with basic information about β Thalassemia including monitoring for pallor, scleral icterus or jaundice, splenomegaly, irritability and decreased energy or feeding.
- 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: only Hemoglobin F is identified, or there is a decrease in the amount of Hemoglobin A. Quantitative assay preferably high performance liquid chromatography (HPLC) demonstrates an Hb F only or decreased HbA pattern. Complete blood count: red blood cell count, mean corpuscular volume, reticulocyte count (with consideration of a smear) are normal at birth but over the first few months of life demonstrate a worsening microcytic anemia with an increasing reticulocyte count. Molecular genetic testing is required to confirm the specific thalassemia genotype.

Clinical Considerations: Newborns with β Thalassemia are generally asymptomatic. Although the CBC may be normal at birth, a severe microcytic anemia develops by six months of age and can present with pallor, jaundice, irritability, failure to thrive, and hepatosplenomegaly. Close monitoring is required to determine if, when, and how regularly transfusions and routine iron chelation therapy are indicated. Without appropriate treatment, complications include failure to thrive, infections, skeletal abnormalities, progressive hepatosplenomegaly, severe iron overload, and premature death. Comprehensive care including family education, a modified immunization schedule, prompt treatment of acute illness, and monitoring for early signs of organ damage reduces morbidity and mortality.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Cooley's Anemia Foundation
Clinicaltrials.gov

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

Find A Hematologist (Filter by Pediatric Hematology-Oncology)
Find a Genetics Clinic Directory
Genetic Testing Registry

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Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	
URL	
Comments	

Local Resource Site (Insert Website Information)

Name	
URL	
Comments	

Appendix *(Resources with Full URL Addresses)*

Additional Information

How to Communicate Newborn Screening Results
- https://bit.ly/NBSResultsHRSA

Gene Reviews
- https://www.ncbi.nlm.nih.gov/books/NBK1426/

Medline Plus
- https://medlineplus.gov/genetics/condition/beta-thalassemia/

Cooley's Anemia Foundation
- https://www.thalassemia.org

Clinicaltrials.gov
- https://clinicaltrials.gov/

Referral (local, state, regional and national)

Find A Hematologist (Filter by Pediatric Hematology-Oncology)
- https://www.hematology.org/education/patients/find-a-hematologist

Find a Genetics Clinic Directory
- https://clinics.acmg.net

Genetic Testing Registry
- https://www.ncbi.nlm.nih.gov/gtr/