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

ACT Sheet

Newborn Screening ACT Sheet

[FA + Barts present (unquantified)], FAB

Alpha (α) Thalassemia

Differential Diagnosis: α-thalassemia silent carrier (1 α-globin gene deletion), α-thalassemia trait (2 α-globin gene deletions in *cis* or *trans*), Hemoglobin H disease (3 α-globin gene deletions), α-thalassemia major (4 α-globin gene deletions), and non-deletion α-thalassemia (e.g. Hb Constant Spring) with or without the deletion of other genes; prematurity. Hb Barts may be present with a structural hemoglobin variant.

Condition Description: The α-thalassemias are inherited types of red blood cell disorders characterized by abnormal hemoglobin production. The number of dysfunctional α-globin genes correspond directly to the relative decrease in α-globin chain production, resulting in an excess of γ- and β- globin chains. The severity of each disorder depends on the number of α genes affected.

You Should Take the Following Actions:

- Inform the family of the screening result.
- Ascertain clinical status (can range from asymptomatic to anemia, hepatosplenomegaly, and jaundice).
- Consult with newborn screening program for a management plan (coordination with NBS program, pediatric hematology or genetic counselor).
- Evaluate the newborn (can range from asymptomatic to splenomegaly, jaundice, microcytic anemia, indirect hyperbilirubinemia, elevated LDH, decreased haptoglobin).
- Coordinate confirmatory diagnostic testing and management as recommended by a pediatric hematologist or genetic counselor.
- Provide family with basic information about α-thalassemia.
- 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 (FA +Barts or FAB). Quantitative assay, preferably high performance liquid chromatography (HPLC) is used to quantify the amount of hemoglobin Barts present. Complete blood count: the CBC and mean corpuscular volume are characteristically low and are dependent upon the type of alpha thalassemia. Molecular genetic testing is indicated depending on the initial assessments and is required to definitively diagnose and to provide reproductive risk counseling for α-thalassemia trait or silent carriers.

Barts levels decrease rapidly after birth and vary significantly depending upon time of collection and methodology. Diagnostic specificity varies widely between NBS programs. It is essential to work with the State Health Department, thalassemia specialist, and/or genetic counselor on a detailed interpretation and response.

Clinical Considerations: Severity ranges from asymptomatic to critically ill depending on the number of functional α-globin genes and whether other non-deletion variants (e.g. Hb Constant Spring) are present. Management depends on the severity of the diagnosis, ranging from reassurance for α-thalassemia trait or silent carrier to hemolytic anemia, splenomegaly, hepatomegaly, jaundice, bony changes, and may require transfusions if Hb H disease, especially if a non-deletion variant (e.g. Hb Constant Spring) is present. Iron deficiency should be documented before initiating iron supplementation.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse
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

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/NBK1435/

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

Condition Information for Families-HRSA Newborn Screening Clearinghouse
- https://newbornscreening.hrsa.gov/conditions/alpha-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/