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

ACT Sheet

Newborn Screening ACT Sheet

[FA + High Barts Hb (>20-25% Barts) or FAB3)]

Alpha (α) Thalassemia: Hb H Disease

Differential Diagnosis: Hemoglobin H disease (3 α-globin gene deletion), α-thalassemia major (4 α-globin gene deletion), and non-deletion α-thalassemia (e.g. Hb Constant Spring) with deletion of other α-globin genes; prematurity, α-thalassemia trait.

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 degree of chain imbalance.

You Should Take the Following Actions:

- Inform the family of the screening result.
- Ascertain clinical status (hepatosplenomegaly, jaundice).
- Consult with pediatric hematologist immediately.
- Evaluate the newborn (splenomegaly, jaundice, microcytic anemia, indirect hyperbilirubinemia, elevated LDH, decreased haptoglobin).
- Coordinate confirmatory diagnostic testing and management as recommended by a pediatric hematologist.
- 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). Quantitative assay preferably high performance liquid chromatography (HPLC) is used to quantify the amount of hemoglobin Barts present. Complete blood count: The mean corpuscular volume is characteristically low and the red cell count is elevated for hemoglobin level. Molecular genetic testing is required to confirm the diagnosis.

Barts levels at birth vary significantly depending on 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: The severity depends upon the number of the four α-globin genes that are deleted and the presence of other non-deletion variants (e.g. Hb Constant Spring). Hemoglobin Barts above 25% in the newborn suggests hemoglobin H disease, due to deletion or non-deletion variants of 3 of the 4 α-globin genes. Presence of a non-deletional variant (e.g. Hb Constant Spring) leads to a more severe phenotype. Hemolytic anemia, splenomegaly, hepatomegaly, jaundice, bony changes, and eventually iron overload may occur if multiple transfusions are required without adequate iron chelation. Hb H disease is characterized by splenomegaly and anemia and may require transfusions particularly if Hb Constant Spring or another non-deletion variant 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/