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

ACT Sheet

Newborn Screening ACT Sheet

[Hemoglobin FE]

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

Differential Diagnosis: Homozygous Hemoglobin E; Hemoglobin E/Beta Zero (β^0) Thalassemia; Hemoglobin E/Beta Plus (β^+) Thalassemia.

Condition Description: Hemoglobin E/E or Hemoglobin E/β^0 Thalassemia are inherited types of red blood cell disorders characterized by abnormal hemoglobin production. They are due to genetic changes in the beta hemoglobin chain. Although Hb E/E is generally benign, HbE/β^0 Thalassemia has a variable clinical course ranging from moderate anemia to transfusion dependency.

You Should Take the Following Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (newborns are expected to be asymptomatic).
- Evaluate the newborn (newborns are expected to be asymptomatic and have a normal clinical exam. If significant signs or symptoms are identified, it is likely related to a different underlying disorder).
- Consult with pediatric hematologist with expertise in hemoglobin disorders within the first week of life with follow up typically recommended between 2-4 months age (it is unusual to have symptoms before 2-4 months of life).
- Coordinate confirmatory diagnostic testing and management as recommended by specialist.
- Provide family with basic information about Hemoglobin E/E or Hemoglobin E/Beta Zero (β^0) 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 on the newborn screen (F>E). Hemoglobin electrophoresis, isoelectric focusing, or high performance liquid chromatography (HPLC): is used to confirm the newborn screening result. Complete blood count (with focus on hemoglobin, mean corpuscular volume, smear, and reticulocyte count): may be normal at birth but may demonstrate a microcytic anemia as early as two months of life. Molecular genetic testing: is required to confirm the diagnosis and to distinguish homozygous Hb E/E from Hb E/β^0 Thalassemia.

Clinical Considerations: While hemoglobin E/E is clinically benign, Hb E/β^0 Thalassemia has a variable presentation. Most individuals with Hb E/β^0 Thalassemia have moderately severe anemia, hepatosplenomegaly, intermittent jaundice, growth restriction, and overexpansion of the bone marrow. Severely affected individuals require life-long transfusion, possible splenectomy, and treatment for iron overload. Monitoring will vary depending on the specific diagnosis and should be done under the direction of a pediatric hematologist. Iron supplements should be avoided unless iron deficiency is documented.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
GARD
Condition Information for Families- HRSA Newborn Screening Clearinghouse
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/NBK1426/

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

GARD
- https://rarediseases.info.nih.gov/diseases/2641/hemoglobin-e-disease

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

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

Referral (local, state, regional and national)

Find A Hematologist (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/