Interpretation of Newborn Hemoglobin Screening Results

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Purpose of Hemoglobin Screening in Newborns

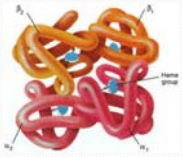
- **Early diagnosis of sickle cell disease**
  - The first manifestations of sickle cell disease in infants may be life-threatening complications:
    - Pneumococcal sepsis
    - Splenic sequestration
- **Early intervention in infants at risk for sickle cell disease will significantly improve their outcome** through:
  - Penicillin prophylaxis
  - Aggressive management of fevers
  - Parental education on splenic sequestration

Methodology

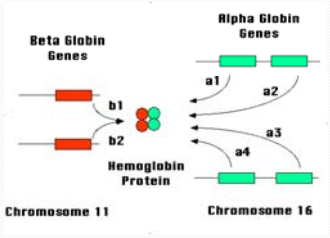
- High performance liquid chromatography
- Identifies different types of hemoglobin
  - Relevant for sickle cell disease:
    - Hgb S ,
    - Hgb C
  - Incidental findings:
    - Hgb H,
    - Hgb Bart's,
    - Hgb E, D, etc.

Hemoglobin

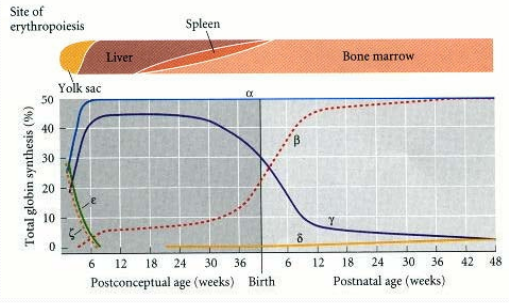
- **Normal variants**
  - Embrionic
  - Fetal $\alpha_2 \gamma_2$
  - Adult 1 $\alpha_2 \beta_2$
  - Adult 2 $\alpha_2 \delta_2$
- **Abnormal variants**
  - S, D, C, E : abn. β chain
  - Barts: γ_4
  - **H:** β_4



Globin Genes



Hemoglobin Switching during development



Normal newborn

- Screening test: FA
- Hemoglobin electrophoresis:
  - Hgb F 60-90%
  - Hgb A1 10-40%
  - Hgb A2 < 1 %

Sickle Cell Syndromes

Screening test	Diagnostic possibilities
FS	**Hgb SS** **Hgb S B_0 thal.** Sickle cell with persistence of fetal Hgb
FSC **FSD**	**Hgb SC** **Hgb SD**
FSA	**Hgb S B_+ thal.** Sickle Cell Trait

Sickle Cell Syndromes: Interventions

- Refer to Pediatric Hematology.
- Evaluate infant and assess for splenomegaly.
- Educate parents/caregivers regarding
  - risk of sepsis , aggressive management of fevers
  - splenic sequestration in Sickle Cell disease
- Pen V K 125 mg po bid until repeat testing confirms or rules out a sickle cell syndrome

Non- Sickle Hemoglobinopathies

Screening test	Diagnosis	Implications
F	β Thalasemia major Premature infant	Severe anemia, may need transfusions Repeat screening
FE	Hemoglobin EE Hgb E β_o Thal.	Mild anemia Moderate top severe anemia
FC	Hemoglobin CC Hgb C β_o Thal.	Mild anemia Mild Anemia

Non- Sickle Hemoglobinopathies Interventions

- **Repeat testing at the age of 2-3 months**
  - **CBC**
  - **Hemoglobin electrophoresis**
- **Family history: looking for anemia, microcytosis**

OR

- **Pediatric Hematology referral**

Alpha Thalassemia Syndromes

Screening test	Diagnosis	Implications
FAB	α Thallsemia	Variable manifestations depending on the number of affected genes Genetic implications

Alpha Thalassemia Syndromes Interventions

- Follow-up tests:
  - CBC, Hemoglobin electrophoresis
    - Microcytosis, Anemia, Hemoglobin Barts
  - Consider alpha globin gene mutation analysis
- Family history
  - Ethnic origin: common in SE Asia
  - History of anemia or microcytosis
- Genetic counseling
- Consider Pediatric Hematology referral

Carriers of Hemoglobin Variants

Screening test	Diagnostic possibilities	Implications
FAS	Sickle Cell Trait	Generally Asymptomatic Genetic implications
FAC	Hemoglobin C trait	Asymptomatic Genetic implications
FAE	Hemoglobin E trait	Asymptomatic / mild anemia Genetic implications
FAV	Variant Hemoglobin	Most likely clinically insignificant

Carriers of Hemoglobin Variants: Interventions

- In general, no medical intervention is needed for the patient
- **Genetic counseling** : asses the risk of having a child with sickle cell disease
  - **For the patient**
    - Genetic counseling when the child reaches adolescence
  - **For the patient's parents**
    - Evaluation of the carrier state : CBC, Hgb electrophoresis
    - Explain the risk the couple has to have a child with sickle cell disease or severe thalassemia

Resources for genetic counseling, newborn screen interpretation

- *www.thalassemia.org*
- *Michigan Department of Community Health*
- *http://www.michigan.gov/documents/finalinterpretation_71834_7.pdf*
- *http://sickle.bwh.harvard.edu/screening.html*

Conclusions

- The aim of newborn screening test for hemoglobin is to identify patients at risk to develop sickle cell disease
- The patterns that are consistent with sickle cell syndromes are **FS, FSC, FSD, FSA**; they should be considered sickle cell disease and treated as such until proven otherwise

Conclusions

- The newborn screening test may identify other hemoglobin abnormalities
  - With possible medical implications: thalassemias
  - With genetic implications
    - For the patient's future children
    - For other children that the patient's parents may have in the future