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
  - Embryonic
  - Fetal $\alpha_2 \gamma_2$
  - Adult 1 $\alpha_2 \beta_2$
  - Adult 2 $\alpha_2 \delta_2$

- Abnormal variants
  - S, D, C, E : abn. $\beta$ chain
  - Bart's: $\gamma^4$
  - H: $\beta^4$

Globin Genes

Hemoglobin Switching during development
Normal newborn

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

Sickle Cell Syndromes

- Screening test

<table>
<thead>
<tr>
<th>Screening test</th>
<th>Diagnostic possibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS</td>
<td>Hgb SS</td>
</tr>
<tr>
<td></td>
<td>Hgb S B_6 thal.</td>
</tr>
<tr>
<td></td>
<td>Sickle cell with persistence of fetal Hgb</td>
</tr>
<tr>
<td>FSC</td>
<td>Hgb SC</td>
</tr>
<tr>
<td>FSD</td>
<td>Hgb SD</td>
</tr>
<tr>
<td>FSA</td>
<td>Hgb S B_6 thal.</td>
</tr>
<tr>
<td></td>
<td>Sickle Cell Trait</td>
</tr>
</tbody>
</table>

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

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

OR

- Pediatric Hematology referral

Non- Sickle Hemoglobinopathies: Interventions

<table>
<thead>
<tr>
<th>Screening test</th>
<th>Diagnosis</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>β Thalasemia major</td>
<td>Severe anemia, may need transfusions</td>
</tr>
<tr>
<td></td>
<td>Premature infant</td>
<td>Repeat screening</td>
</tr>
<tr>
<td>FE</td>
<td>Hemoglobin EE</td>
<td>Mild anemia</td>
</tr>
<tr>
<td></td>
<td>Hgb E β, Thal.</td>
<td>Moderate to severe anemia</td>
</tr>
<tr>
<td>FC</td>
<td>Hemoglobin CC</td>
<td>Mild anemia</td>
</tr>
<tr>
<td></td>
<td>Hgb C β, Thal.</td>
<td>Mild Anemia</td>
</tr>
</tbody>
</table>

Alpha Thalassemia Syndromes

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<tr>
<th>Screening test</th>
<th>Diagnosis</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAB</td>
<td>α Thalasemia</td>
<td>Variable manifestations depending on the number of affected genes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genetic implications</td>
</tr>
</tbody>
</table>
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

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<th>Implications</th>
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</thead>
<tbody>
<tr>
<td>FAS</td>
<td>Sickle Cell Trait</td>
<td>Generally Asymptomatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genetic implications</td>
</tr>
<tr>
<td>FAC</td>
<td>Hemoglobin C trait</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genetic implications</td>
</tr>
<tr>
<td>FAE</td>
<td>Hemoglobin E trait</td>
<td>Asymptomatic / mild anemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genetic implications</td>
</tr>
<tr>
<td>FAV</td>
<td>Variant Hemoglobin</td>
<td>Most likely clinically insignificant</td>
</tr>
</tbody>
</table>

Carriers of Hemoglobin Variants: Interventions

- In general, no medical intervention is needed for the patient
- Genetic counseling: assess 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://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