17. SICKLE CELL SCREENING AND SELECT TOPICS IN PREVENTION OF COMPLICATIONS

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We used the following sources to construct indicators for sickle cell disease screening for newborns and selected topics in prevention of complications for infants and children: appropriate chapters from textbooks on pediatrics (Martin and Pearson in Oski et al., 1994) and pediatric primary care (Platt in Dershewitz, 1993; Whitten in Hoekelman et al., 1992) and the Agency for Health Care Policy and Research (AHCPR) clinical practice guideline Sickle Cell Disease: Screening, Diagnosis, Management, and Counseling in Newborns and Infants (Sickle Cell Disease Guideline Panel, 1993).

IMPORTANCE

There are several types of sickle cell diseases, among them sickle cell anemia (Hb SS), hemoglobin SC disease (Hb SC), and sickle beta-thalassemia. In the United States, these diseases are most commonly found in people of African ancestry, but they also affect people of Mediterranean, Caribbean, South and Central American, Arabian, and East Indian ancestry. In the United States, sickle cell anemia affects more than 50,000 people and occurs in about 1 in 375 African-American live births. Estimated prevalence of hemoglobin SC disease is 1 in 835 African-American live births; for sickle beta-thalassemia, it is 1 in 1,667 African-American live births (Sickle Cell Disease Guideline Panel, 1993).

EFFICACY/EFFECTIVENESS OF INTERVENTIONS

Screening

The AHCPR practice guideline recommends screening of all newborns for sickle cell disease regardless of racial or ethnic background. The rationale is (1) there is a benefit to screening (prophylaxis, which is discussed below), (2) it is not possible to identify accurately a person's heritage by appearance or surname, and (3) much screening is
conducted by state-sponsored programs supported at least in part by public funds. More than 40 states, the District of Columbia, Puerto Rico, and the Virgin Islands conduct universal newborn hemoglobinopathy screening (Sickle Cell Disease Guideline Panel, 1993).

The Sickle Cell Disease Guideline Panel (1993) states that screening of populations with a low prevalence of sickle cell disease is cost-effective when the screening is integrated into a laboratory that is also testing samples from a population with a high prevalence. In states that provide universal screening, all managed care plans should conduct the screening and obtain the results. However, low prevalence states that do not have universal screening programs may not provide access to laboratories in high prevalence areas. Therefore, managed care plans that serve low prevalence populations in these states might decide that it is not cost-effective to screen all newborns. However, there would probably be little disagreement that they should be screening all African-American newborns.

Platt (in Dershewitz, 1993), Whitten (in Hoekelman et al., 1992), and Martin and Pearson (in Oski et al., 1994) all recommend hemoglobin electrophoresis for definitive diagnosis. The Sickle Cell Disease Guideline Panel (1993) lists three methods that can be used to make a definitive diagnosis: electrophoresis, immunologic testing, or DNA analysis. The panel also says that testing both parents' blood can assist in diagnosis. Some types of sickle cell disease do not need confirmation (e.g., Hb SE, Hb SD, or Hb S\textsubscript{Arab}), but these forms of the disease are quite rare (Sickle Cell Disease Guideline Panel, 1993). Whitten (in Hoekelman et al., 1992) says that parents generally do not need to be tested when a child is found to have sickle cell disease since the diagnosis is usually clear.

If a child has a positive screen at birth, it should be repeated after the child is at least one month old (unless both parents have sickle trait) since the initial test could also have detected hereditary persistence of fetal hemoglobin or sickle cell-beta thalassemia (Whitten in Hoekelman et al., 1992). While Platt (in Dershewitz, 1993) does not give a specific timetable for screening, she states that diagnosis should be made in the newborn period.
Prophylaxis

Infections with *Streptococcus pneumoniae* are one of the major causes of death in infants with sickle cell anemia. Without prophylaxis, about 30 percent will become infected during the first three years of life, and about one-third of them will die from infection (Gaston and Verter, 1990). This occurs because of functional asplenia that develops over the first two years of life (Sickle Cell Disease Guideline Panel, 1993). A randomized, controlled clinical trial showed that twice-daily oral penicillin reduces the morbidity and mortality from *Streptococcus pneumoniae* infections in children with sickle cell disease (Gaston et al., 1986).

The Sickle Cell Disease Guideline Panel (1993) recommends beginning penicillin prophylaxis by 2 months of age for infants with suspected sickle cell anemia and sickle beta-thalessemia, whether or not definitive diagnosis has been made yet. Martin and Pearson (in Oski et al., 1994), however, say that prophylaxis should begin by 6 months of age (Martin and Pearson in Oski et al., 1994), and the American Academy of Pediatrics (AAP) (in Peter, 1994) says it should begin before 4 months. Platt (in Dershewitz, 1993) says that it should begin as soon as possible.

While there is general support for the use of penicillin prophylaxis, there is some disagreement on the age at which it can be discontinued. Some state that prophylaxis should continue twice a day for the first five years of life (Platt in Dershewitz, 1993; Whitten in Hoekelman et al., 1992), while at least one other states that it should continue until at least 6 years of age (Martin and Pearson in Oski et al., 1994). The AAP (in Peter, 1994) says that prophylaxis should be strongly considered in children younger than 5 years old and considered for older children. Research to determine the age at which to discontinue prophylaxis is currently being conducted (AAP in Peter, 1994).

Children with sickle cell disease should receive the pneumococcal vaccine when they are at least two years old (AAP in Peter, 1994; Platt, in Dershewitz, 1993).
Monitoring

Children of all ages with sickle cell disease should be seen every few months to monitor baseline laboratory data such as complete blood cell count and reticulocyte count and to monitor intercurrent events (Platt, in Dershewitz, 1993).
### Recommended Quality Indicators for Sickle Cell Screening for Newborns and Prevention of Complications

The following criteria apply to sickle cell screening for newborns and select topics in prevention of complications for infants and children.

**Screening**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of Evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1. All children in states with mandatory newborn sickle cell testing should be screened before hospital discharge or within 48 hours of birth, whichever comes later.</td>
<td>III</td>
<td>Inferred from Sickle Cell Disease Guideline Panel, 1993</td>
<td>Prevent pneumococcal infection. Decrease heart failure from splenic sequestration.</td>
<td>Screening allows for early diagnosis and prophylactic therapy (e.g., penicillin) before the patient develops the first pneumococcal infection. It also enables monitoring (which helps treatment of sickle crises) to begin. It allows time to teach the family about symptoms to watch for in children with sickle cell.</td>
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<td>2. African-American children should be tested for sickle cell disease by the end of the third month of life.</td>
<td>III</td>
<td>Whitten, in Hoekelman et al., 1992</td>
<td>Prevent pneumococcal infection. Decrease heart failure from splenic sequestration.</td>
<td>Though the AHCPR guideline recommends testing for all newborns regardless of race or ethnicity, it also says that universal testing has only been shown to be cost-effective when low prevalence states coordinate with high prevalence regions. However, individual managed care organizations located in states that do not offer universal screening may not consider it cost-effective to test all newborns and may not have the ability to coordinate with high prevalence states. Testing through a state newborn screening program is adequate if results are noted in the chart. This indicator will be difficult to operationalize if racial background is not typically recorded in the chart.</td>
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<td>3. Children with a positive sickle screen at less than or equal to one month of age should have a repeat screen after one month of age and prior to the end of six months of age.</td>
<td>III</td>
<td>Sickle Cell Disease Guideline Panel, 1993; Whitten, in Hoekelman et al., 1992</td>
<td>Prevent allergic reactions from antibiotics. Prevent antibiotic resistance. Improve quality of life.</td>
<td>Confirmatory tests are necessary because of the possibility of false positive diagnoses. False positive diagnoses lead to unnecessary prophylaxis and vigilance for symptoms. Prophylactic antibiotics can have side effects, increase resistance in the community, and are disruptive to take on a daily basis. The purpose is to confirm the diagnosis.</td>
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<td>4. Children with a positive sickle screen or children suspected of being positive for sickle cell disease should be placed on daily penicillin prophylaxis from at least six months of age until at least five years of age.</td>
<td>I</td>
<td>Gaston et al., 1986; AAP, in Peter, 1994; Martin &amp; Pearson, in Oski et al., 1994; Platt, in Dershewitz, 1993; Sickle Cell Disease Guideline Panel, 1993</td>
<td>Prevent pneumococcal infections.</td>
<td>Pneumococcal infections are prevalent and are often fatal in persons with sickle cell disease. The references recommend different age ranges for prophylaxis. The one specified here is the narrowest found in the reviewed literature.</td>
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<td>5. Children with sickle cell disease should have a hematocrit or hemoglobin, and reticulocyte count performed at least every four months.</td>
<td>III</td>
<td>Platt, in Dershewitz, 1993</td>
<td>Prevent worsening anemia and death. Improve quality of life. Decrease heart failure from splenic sequestration.</td>
<td>This information provides baseline values for comparison during periods of acute illness. It also allows determination of when the patient is more anemic than baseline so that he/she can receive potentially life-saving transfusions, and it avoids inappropriate transfusion by clinicians who do not recognize that the patient is at a stable level of anemia.</td>
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<td>6. Children with sickle cell disease should have received the pneumococcal vaccine between 2 years and 3 years of age.</td>
<td>III</td>
<td>Inferred from AAP in Peter, 1994; Platt, in Dershewitz, 1993</td>
<td>Prevent pneumococcal infections.</td>
<td>The literature does not say how soon after the second birthday one should receive this vaccine, but it seems clear that the sooner the better to prevent possible infection.</td>
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<td>7. A child older than 2 years with sickle cell disease who joins a new managed care organization should have documented at the first visit whether or not he/she has ever had a pneumococcal vaccine or that efforts are being made to determine the vaccine history.</td>
<td>I, III</td>
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<td>Prevent pneumococcal infections.</td>
<td>This is not specifically recommended, but the importance of this vaccine suggests that it should be addressed immediately by new providers.</td>
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<td>8. The patient should receive the vaccination within one month of this visit if the patient or the patient's caregiver does not know if the vaccine has been given and it has not been confirmed by other means. If the patient or patient's caregiver does not believe the vaccine had been given before, the vaccine should be given at that visit.</td>
<td>I, III</td>
<td>Hales and Barriere, 1979; Ammann et al., 1977</td>
<td>Prevent pneumococcal infections.</td>
<td>This is not specifically recommended, but the importance of this vaccine suggests that it should be addressed immediately by new providers.</td>
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Quality of Evidence Codes:
I: RCT
II-1: Nonrandomized controlled trials
II-2: Cohort or case analysis
II-3: Multiple time series
III: Opinions or descriptive studies
REFERENCES – SICKLE CELL SCREENING FOR NEWBORNS


