Sickle Cell Disease

BACKGROUND

Cause and Diagnosis of SCD

Sickle cell disease (SCD) is a group of inherited red blood cell disorders. Present at birth, SCD is inherited when a child receives two sickle cell genes—one from each parent. Healthy red blood cells are round, and they move through small blood vessels to carry oxygen to all parts of the body. Conversely, red blood cells in individuals with SCD become hard and sticky, resembling a C-shaped farm tool called a ‘sickle’. These cells die early causing a constant shortage of red blood cells. They may also become stuck as they move through small blood vessels and thus obstruct blood flow. Pain and other serious effects such as infection, acute chest syndrome and stroke may occur. (1CDC, 2014).

A simple blood test is used to diagnose SCD and is often during routine newborn screening tests at the hospital however, SCD can be diagnosed before birth. Early diagnosis and treatment is important as children with SCD are at an increased risk of infection and other health problems. The most common types of SCD (1CDC, 2014) include:

- **HbSS** is the most severe form of SCD, occurring in those who inherit one sickle cell gene (‘S’) from each parent.
- **HbSC** is a milder form of SCD and is found in those who inherit a sickle cell gene (‘S’) from one parent and a gene for an abnormal hemoglobin called ‘C’ from the other parents.
- **HbS beta thalassemia** occurs when one inherit one sickle cell gene (‘S’) from one parent and one gene for beta thalassemia from the other parent. There are two types of beta thalassemia: ‘0’ and ‘+’. Individuals with **HbS beta 0-thalassemia** usually have a severe form of SCD; those with **HbS beta +-thalassemia** may have a milder form.
- **HbSD, HbSE, and HbSO** are rare types of SCD and are found in those who inherit one sickle cell gene (‘S’) and one gene from an abnormal type of hemoglobin (‘D’, ‘E’, or ‘O’).

**HbAS** is found in individuals who have a sickle cell trait and inherit one sickle cell gene (‘S’) from one parent and one normal gene (‘A’) from the other parent. This is also known as sickle cell trait (SCT) – individuals with SCT usually do not have any of the signs of the disease and live a normal life, but can pass the trait on to their children (CDC, 2013).

- If both parents have SCT, there is a 50% chance that any child of theirs also will have SCT. Such children will not have symptoms of SCD, but they can pass SCT on to their children.
- If both parents have SCT, there is a 25% (or 1 in 4) chance that any child of theirs will have SCD. There is the same 25% (or 1 in 4) chance that the child will not have SCD or SCT.
- If one parent has SCT, there is a 50% (or 1 in 2) chance that any child of this parent will have SCT and an equal 50% chance that the child will not have SCT.

Screening

The U.S. Preventive Services Task Force (USPSTF) (2007) recommends screening for sickle cell disease in newborns (Grade: A Recommendation).
Complications of SCD

Symptoms of SCD vary and typically begin during the first year of life, approximately around 5 months of age. Treatment options are different for each person depending on the symptoms. The only cure for SCD is a bone marrow or stem cell transplant. Common complications include:

- Hand-Foot Syndrome
- Pain "Episode" or "Crisis"
- Anemia
- Infection
- Acute Chest Syndrome
- Splenic Sequestration
- Vision Loss
- Leg Ulcers
- Stroke
- Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

Other possible complications of SCD include:

- Damage to body organs (like the liver, heart, or kidneys), tissues, or bones due to a lack of blood flow
- Malnutrition / growth retardation among adolescents can cause a delayed onset of puberty; infertility in males
- Gallstones
- Painful erection of the penis (priapism) can last ≤ 2 hours or ≥ 4 hours and may lead to impotence

Who Has SCD?

Sickle cell disease (SCD) affects millions of people worldwide and is particularly common among those of whose ancestors came from sub-Saharan Africa; Spanish-speaking regions in the Western Hemisphere (South America, the Caribbean, and Central America); Saudi Arabia; India; and Mediterranean countries such as Turkey, Greece, and Italy. (CDC, 2011). SCD affects 90,000 to 100,000 Americans and it is estimated among:

- 1 out of every 500 Black or African-American births.
- 1 out of every 36,000 Hispanic-American births.
- 1 in 12 Blacks or African Americans.

SCD is a major public health concern. From 1989 through 1993, an average of 75,000 hospitalizations due to SCD occurred in the United States, costing approximately $475 million.

Sickle cell-related death among Black or African-American children under age 4 years fell by 42% from 1999 through 2002. The drop coincided with the introduction in 2000 of a vaccine protecting against invasive pneumococcal disease.

Special Considerations for Pediatric Members

In 2011, the American Academy of Pediatrics reaffirmed their 2002 guideline. Health maintenance for pediatric members should be comprehensive, ensuring the following are discussed:

- Prophylactic medications
- Immunizations
- Comprehensive medical evaluation
- Psychosocial care
The AAP (2002) recommends that health supervision should consist of family education, health maintenance, acute illness and psychosocial care.

### Family Education

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<tr>
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<tbody>
<tr>
<td>1. Review disease manifestations and the parents’ response.</td>
<td>2. Review importance of penicillin prophylaxis, if applicable, and of urgent medical evaluation for and treatment of febrile illness (temperature &gt; 38.5°C).</td>
<td>3. Review signs, symptoms, and management of splenic sequestration and other anemic crisis, dactylitis and other manifestations of pain, acute chest syndrome.</td>
<td>4. Review home management of painful events.</td>
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<td>5. Discuss CNS manifestations of SCD, stressing the importance of urgent evaluation for signs or symptoms suggestive of stroke or transient ischemic attack (TIA). Discuss screening w/ TCD ultra-sonography, if available.</td>
<td>6. Discuss enuresis and its relationship to SCD (if applicable).</td>
<td>7. Recommend no exposure to pet reptiles to decrease the risk of salmonellosis.</td>
<td>8. Reinforce the rationale and importance of periodic comprehensive evaluations.</td>
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<td>9. Discuss options for adult-oriented health care providers and develop with the patient a plan for transition from pediatric to adult medical care.</td>
<td>10. Reconsider patient's medical home model depending on family preference, frequency / severity of complications.</td>
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<th>Age 5 to 13 (Late Childhood)</th>
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<td>12. Reinforce anticipatory guidance regarding anemic crisis (e.g., splenic sequestration for patients with HbSC and S beta-thalassemia), acute chest syndrome, stroke, and TIA.</td>
<td>12. Provide anticipatory guidance regarding anemic crisis (e.g., splenic sequestration for HbSC and S beta-thalassemia), acute chest syndrome, stroke, TIA, and priapism.</td>
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<td>13. For boys, discuss priapism, initial home management, and seeking urgent evaluation and treatment of prolonged episodes.</td>
<td>13. Discuss sexuality and the availability of contraception options, such as barriers, intramuscular medroxyprogesterone, and low-dose estrogen oral contraceptives.</td>
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<td>14. Discuss genetics, including partner testing, genetic counseling, and prenatal diagnosis.</td>
<td>14. Discuss the importance of avoiding drugs and alcohol which may precipitate or exacerbate complications.</td>
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<td>15. Discuss chronic manifestations of the disease (e.g., proliferative retinopathy, cholelithiasis, avascular necrosis of the hip and shoulder, leg ulcers, delayed growth and puberty.</td>
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### Health Maintenance

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<tr>
<td>1. Begin prophylactic administration of penicillin V potassium, 125 mg orally, twice a day, by 2 months of age for infants with HbSS and S beta othalassemia. The routine use of penicillin prophylaxis for infants with HbSC and S beta-thalassemia is controversial.</td>
<td>2. Provide routine immunizations, including Haemophilus influenzae type b (Hib) and 7-valent pneumococcal conjugate vaccines, beginning at 2 months of age. Yearly influenza immunization is recommended for children 6 months and older.</td>
<td>3. Provide comprehensive medical evaluations every 2 to 4 months. Critical issues during the first year include the documentation of spleen size and baseline CBC and reticulocyte counts, which may change significantly as HbF...</td>
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</table>
### Sickle Cell Disease

1. **Levels decrease. Baseline information should be provided to parents. Red blood cell minor antigen phenotype should be determined if transfusions that may be needed for treatment of acute illness can be matched to prevent alloimmunization.**

4. **Develop and modify as needed an individualized patient care plan.**

#### Age 1 to 5 (Early Childhood)

1. *Continue prophylactic administration of penicillin V potassium, 125 mg orally, twice a day, for children with HbSS and S beta-thalassemia. At 3 years of age, increase the dosage to 250 mg orally, twice a day. The routine use of penicillin prophylaxis for children with HbSC and S beta-thalassemia is controversial.*

2. *Complete immunization with Hib and 7-valent pneumococcal conjugate vaccines. Administer the 23-valent pneumococcal polysaccharide vaccine at 2 and 5 years of age but no earlier than 6 to 8 weeks after the last dose of pneumococcal conjugate vaccine. Yearly influenza immunization is recommended.*

3. *Provide comprehensive medical evaluations at least every 6 to 12 months and modify the patient’s care plan as needed. Important issues include growth and development; jaundice; sleep apnea; cardiopulmonary status, including systemic hypertension and functional heart murmurs; spleen size; and neurologic status.*

4. *Document baseline CBC and reticulocyte counts (every 6–12 months for patients with HbSS and S beta-thalassemia and at least yearly for patients with HbSC and S beta-thalassemia).*

5. *Baseline renal and liver function tests, urinalysis, chest radiography, pulse oximetry, electrocardiography, echocardiography, and/or TCD ultrasonography may be indicated.*

#### Age 5 to 13 (Late Childhood)

1. *Continuation of prophylactic administration of penicillin V potassium, 250 mg orally, twice a day, after the fifth birthday may be appropriate in selected patients, including those with a history of invasive pneumococcal infection or surgical splenectomy.*

2. *Administer Hib and 7-valent pneumococcal conjugate vaccines if not previously immunized. Administer second 23-valent pneumococcal polysaccharide vaccine at 5 years of age but no earlier than 3 years after the first pneumococcal polysaccharide vaccine and 6 to 8 weeks after the last pneumococcal conjugate vaccine. A third dose of pneumococcal polysaccharide vaccine may be given no earlier than 5 years after the second pneumococcal polysaccharide vaccine and 6 to 8 weeks after the last pneumococcal conjugate vaccine. Yearly influenza immunization is recommended.*

3. *Provide comprehensive medical evaluations every 6 to 12 months and modify the patient’s care plan as needed. Important issues include growth and development; sleep apnea; cardiopulmonary status, including systemic hypertension and functional heart murmurs; hepatosplenomegaly; cholelithiasis; proteinuria; pubertal development; enuresis; avascular necrosis of the hip and shoulder; and neurologic status. Screening for proliferative retinopathy with periodic retinal examinations beginning at 10 years of age is often recommended, especially for patients with HbSC.*

4. *Document baseline CBC and reticulocyte counts at least yearly.*

5. *Baseline pulse oximetry, renal and hepatic function tests, chest radiography, pulmonary function tests, electrocardiography, echocardiography, and/or TCD ultrasonography may be indicated.*

6. *Abdominal ultrasonography to detect cholelithiasis may be indicated.*

#### Age 13 to 21 (Adolescence to Early Adulthood)

1. *Yearly influenza immunization is recommended.*

2. *Provide comprehensive medical evaluations every 6 to 12 months and modify the patient’s care plan as needed. Important issues include adolescent maturation and development; sleep apnea; cardiopulmonary status, including systemic hypertension, restrictive lung disease, and pulmonary hypertension; hepatosplenomegaly; cholelithiasis; proteinuria; pubertal development; avascular necrosis; and neurologic status. Periodic retinal examinations are often recommended, especially for patients with HbSC.*
3. Document baseline CBC and reticulocyte counts at least yearly.

4. Baseline pulse oximetry, renal and liver function tests, chest radiography, pulmonary function tests, electrocardiography, and/or echocardiography may be indicated.

5. Abdominal ultrasonography to detect cholelithiasis may be indicated.

### Acute Illness

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<th>Birth to Age 1 (Infancy)</th>
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<tr>
<td>1. Develop a plan for around-the-clock access to a medical facility that can provide urgent evaluation for and treatment of acute illness characterized by fever (temperature greater than 38.5°C), pallor, lethargy, abdominal distention or enlarging spleen size, or tachypnea or other signs of respiratory illness.</td>
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<td>2. Arrange immediate access at the acute care facility to baseline information about the patient.</td>
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<td>3. Anticipate and address any insurance barriers to the receipt of appropriate care for acute illness.</td>
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### Psychosocial Care

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<td>1. Explore personal beliefs about illness and existing sources of stress and support.</td>
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<td>2. Review insurance coverage and provide assistance with application for public support, if applicable.</td>
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<td>3. Discuss transportation issues, particularly for episodes of acute illness.</td>
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<td>4. Provide information regarding support groups and other community-based organizations.</td>
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<td>5. Discuss child care or preschool arrangements and offer to assist in educating child care providers or educators about SCD.</td>
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<td>5. Review school attendance and performance and consider formal neurocognitive testing.</td>
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<td>6. Offer assistance with education of school personnel about SCD.</td>
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<td>7. Discuss educational and vocational goals.</td>
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Providers shall educate the member and their parent/guardian of the following acute and chronic manifestations, including how the member should proceed if symptoms occur (e.g., emergency room vs. calling the provider):

**Acute Manifestations**
- Bacterial sepsis*
- Recurrent vaso-occlusive pain (dactylitis, musculoskeletal or abdominal pain)
- Splenic sequestration*
- Aplastic crisis*
- Acute chest syndrome*
- Stroke*
- Priapism
- Hematuria, including papillary necrosis

**Chronic Manifestations**
- Anemia
- Jaundice
- Splenomegaly
- Functional asplenia
- Cardiomegaly and functional murmurs
- Hyposthenuria and enuresis
- Proteinuria
- Cholelithiasis
- Delayed growth and sexual maturation
* Potential cause of mortality

- Restrictive lung disease
- Pulmonary hypertension
- Avascular necrosis
- Proliferative retinopathy
- Leg ulcers
- Transfusional hemosiderosis

**Member Education**

| Source |  
|--------|---|
| CDC, 2014 | CDC, 2010 |
| CDC, 2010 |  

Individuals with SCD have less access to comprehensive team care than people with genetic disorders such as hemophilia and cystic fibrosis. It is important for providers to talk to members with SCD, emphasizing that one can live a full life and enjoy most activities that other people do. Providers shall educate members of the following:

**Regular health checkups** with a primary care physician (PCP) may prevent serious complications of the disease:

- Babies from birth to 1 year of age should see a doctor every 2 to 3 months
- Children from 1 to 2 years of age should see a doctor at least every 3 months
- Children and adults from 2 years of age or older should see a doctor at least once every year

**Infection Prevention** should be stressed to members as common illnesses like the flu can be dangerous for someone with SCD. They should limit exposure to family or friends who may be sick as well as practice good hand washing when cooking or eating food. In addition, hand washing should occur upon one:

- Blowing their nose, coughing, or sneezing
- Shaking hands
- Touching people or things that can carry germs (e.g., diapers or toilets, raw meat and eggs, unwashed vegetables, animals, animal waste, trash or a sick person)

**Emergency Treatment** should be discussed with members. Providers can instruct individuals with SCD to proceed to an emergency room or urgent care facility when any of the following occur:

- Fever above 101° F
- Difficulty breathing
- Chest pain
- Abdominal (belly) swelling
- Severe headache
- Sudden weakness or loss of feeling and movement
- Seizure
- Painful erection of the penis that lasts more than 4 hours
- Pain anywhere in the body that will not go away with treatment at home
- Any sudden problem with vision

**Food Safety** is important to reduce the chance of bacteria (salmonella) being ingested. Members should be mindful of the following when cooking and eating:

- Wash hands, cutting boards, counters, knives, and other utensils after they touch uncooked foods
- Wash vegetables and fruit well before eating them
- Cook meat until it’s well done. The juices should run clear and there should be no pink inside
- Do not eat raw or undercooked eggs; be mindful of things raw eggs might be in (e.g., sauces, cookie dough)
- Do not eat raw or unpasteurized milk or other dairy products; labels should say “pasteurized”

**Reptiles** may also transmit salmonella; children should limit or eliminate exposure to turtles, snakes, and lizards.

**Acetaminophen Use.** In August 1, 2013, the U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that acetaminophen has been associated with a risk of rare but serious skin reactions (AHRQ, 2012). These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized
Exanthematous pustulosis (AGEP), can be fatal. Reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions.

**Vaccines** can prevent many infections in children with SCD. Members benefit from regularly scheduled vaccines and the:

- Flu vaccine (influenza vaccine) every year after 6 months of age
- A special pneumococcal vaccine (called 23-valent pneumococcal vaccine) at 2 and 5 years of age
- Pneumococcal conjugate vaccine (PCV13) between 6 and 18 years of age, if the child hasn’t previously received the vaccine
- Meningococcal vaccine, if recommended by a doctor

NOTE: Adults should receive the flu vaccine every year, as well as the pneumococcal vaccine and any others recommended by a doctor.

**Penicillin** use is also an option for individuals with SCD. Penicillin (or other antibiotic prescribed by a doctor) may be used in children every day until at least 5 years of age.

For additional information, Providers may wish to refer Members to the following Centers for Disease Control and Prevention website at [http://www.cdc.gov/ncbddd/sicklecell/freematerials.html](http://www.cdc.gov/ncbddd/sicklecell/freematerials.html) In addition, parents or caregivers of children may find benefit in the CDC booklet *Tips for Supporting Students with Sickle Cell Disease* available at [http://www.cdc.gov/ncbddd/sicklecell/documents/tipsheet_supporting_students_with_scd.pdf](http://www.cdc.gov/ncbddd/sicklecell/documents/tipsheet_supporting_students_with_scd.pdf)

**REFERENCES**


National Heart, Lung and Blood Institute. (2002). The management of sickle cell disease. Retrieved from
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HS-1038


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MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<tr>
<td>6/17/2014</td>
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