Sickle Cell Disease

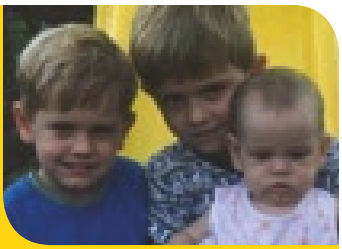
In the United States, sickle cell disease occurs in approximately 1 in 2,500 newborns. It is more prevalent than any other condition identified by newborn blood screening.

I. What is Sickle Cell Disease?

Sickle cell disease (SCD) is the term used to refer to a group of complex genetic disorders variably characterized by anemia; severe pain; potentially life-threatening complications such as bacterial septicemia, splenic sequestration, acute chest syndrome, stroke, and chronic organ damage. These and other clinical manifestations result from chronic hemolysis and intermittent episodes of vascular occlusion that cause tissue injury and organ dysfunction. SCD is inherited in an autosomal recessive manner. Heterozygous individuals (carriers) have sickle cell trait, a generally benign, asymptomatic genetic carrier state. Homozygous and compound heterozygous individuals have symptomatic disease. Four genotypes – sickle cell anemia (HbSS), sickle-hemoglobin C disease (HbSC), and two types of sickle β-thalassemia (sickle β+-thalassemia and Sβ°-thalassemia) – account for most SCD in the United States.

II. What is the Incidence of Sickle Cell Disease?

It is estimated that over 2 million Americans are genetic carriers of SCD and that 70-80,000 Americans have sickle cell disease.[1,2] A common misperception is that SCD affects only people of African ancestry, however, SCD can affect persons of any race or ethnicity. Genes for SCD are common in persons of African, Mediterranean, Middle Eastern, and Indian ancestry and persons from the Caribbean and parts of Central and South America. SCD occurs in approximately 1 in 350 African-Americans. Overall, the prevalence of SCD in US newborns is 1 in 2,000-2,500, greater than that of any other condition detected by newborn blood screening.



"Sickle Cell Disease can affect ANY race! My husband and I are a Caucasian couple with 3 beautiful children that have sickle beta plus thalassemia. I am of Italian decent and have thalassemia trait. When I was pregnant I was tested and my doctor wanted to test my husband for it as well. I received a call several days later that he had sickle trait. I said, 'No way! My husband has blonde hair and blue eyes.' We *thought* at the time that this disease was **only** a black disease. We now have 2 sons and 1 daughter that have sickle beta plus thalassemia, one with blonde hair and blue eyes."

III. Sickle Cell Disease in Children: The Importance of Early Diagnosis and Treatment

A demonstration in 1986 that prophylactic penicillin markedly reduces the incidence of pneumococcal sepsis provided a strong rationale for the widespread implementation of newborn screening for SCD. Newborn screening, when linked to timely diagnostic testing, parental education, and comprehensive care, markedly reduces morbidity and mortality from SCD in infancy and early childhood. In 1987, a consensus panel recommended "universal screening of all newborns for hemoglobinopathies."[3]

Currently, 47 states, the District of Columbia, Puerto Rico, and the Virgin Islands provide universal newborn screening for SCD. Screening is available only by request in the other three states, although universal screening is provided for disorders (e.g. classical galactosemia) estimated to be less common in those states than SCD. Screening by request is problematic because infants with SCD often escape testing.

IV. Sickle Cell Disease Fever Alert

Because children with SCD develop functional asplenia as early as 3 months of age, fulminant infection with S pneumoniae and other encapsulated bacteria is the most common cause of death in infancy and childhood. Thus, immunization with pneumococcal conjugate and polysaccharide vaccines, penicillin prophylaxis, and education about the importance of urgent evaluation of all illness with temperature greater than 38.5˚C are critical. Evaluation and treatment of fever includes rapid triage and physical assessment, urgent CBC and reticulocyte counts, blood culture (plus cerebrospinal fluid analysis and other cultures as indicated), and prompt administration of a broad-spectrum parenteral antibiotic, such as ceftriaxone. The presence of a focus of infection (e.g., viral upper respiratory illness, otitis media) does not alter the urgency of administering parenteral antibiotics. Because of the prevalence of resistant pneumococci, vancomycin should be added for proven or suspected meningitis and other severe illness. Other potentially life-threatening complications, such as splenic sequestration and acute chest syndrome, often occur with fever.

V. Interpreting Newborn Screening Results for Sickle Cell Disease

Hemoglobins identified by newborn screening are generally reported in order of quantity. Because more fetal hemoglobin (Hb F) than normal adult hemoglobin (Hb A) is present at birth, the screening test result for most normal infants is FA. Infants with hemoglobinopathies also show a predominance of Hb F at birth. Those with SCD show Hb S in absence of Hb A (FS), Hb S with another hemoglobin variant (e.g., FSC) or a quantity of Hb S greater than Hb A (FSA). In contrast, carriers of hemoglobin variants (ie hemoglobin traits) have more Hb A than the variant (e.g. FAS, FAC, FAE). Hundreds of other Hb variants may also be identified. Most of these less common variants are associated with few or no clinical consequences. Many screening programs also detect and report Hb Bart's, indicative of I thalassemia. Guidelines for follow-up of infants with positive screening results have been published.[1,4]

Whenever an infant has a potentially clinically significant abnormal hemoglobin screening result, repeat testing of a liquid blood sample is needed for confirmation.

VI. The Medical Home for Children with Sickle Cell Disease and Carriers of Hemoglobin Variants

As part of your clinical practice, you may provide care for children with sickle cell disease or for those who are genetic carriers of hemoglobinopathies.

Children with Sickle Cell Disease

Every child with SCD should receive comprehensive care that is provided and coordinated through an appropriate medical home. For many patients, the most appropriate medical home is a multidisciplinary sickle cell clinic that coordinates all aspects of comprehensive care in collaboration with the child's primary care provider. In other cases, the medical home may be provided by a knowledgeable primary care physician with periodic referrals to sickle cell specialists for comprehensive evaluations and for management of severe complications.

The primary components of comprehensive care of sickle cell disease[2] include:

- Family and patient education
- Health maintenance including prophylactic medications, immunizations, comprehensive medical evaluations, and management of chronic complications
- Around-the-clock access to appropriate treatment of acute illness
- Psychosocial care
- Genetic education and counseling

Genetic Carriers of Hemoglobin Variants (e.g. Sickle Cell Trait)

Parents of infants who are detected to be carriers of hemoglobin variants should be offered appropriate education, counseling, and testing. Education of families whose infants have hemoglobin S, C, or E trait should emphasize the benign nature of genetic carrier states and the fact that no restrictions of physical activity are indicated. Counseling should include review of autosomal recessive inheritance and the availability of carrier testing for parents and other family members to identify couples at risk for children with SCD or other hemoglobinopathies.

VII. For Additional Information

For additional information about sickle cell disease, please refer to the following documents and Web sites:

- National Center of Medical Home Initiatives (NCMHI): www.medicalhomeinfo.org

This Web site contains the AAP endorsed Sickle Cell Disease toolkit as well as a wealth of resources and links about newborn screening and integration into the medical home. In addition, NCMHI provides support and technical assistance to physicians, families, and other medical and non-medical providers who care for children with special needs so that they have access to a medical home.

- National Institutes of Health. (2002). The Management of Sickle Cell Disease. NIH Publication No. 02-2117.

This is an inexpensive ($5.00), easy-to-read book that covers all aspects of care for children and adults who have sickle cell disease. The text covers newborn screening, and also includes a chapter on sickle cell trait. It can be downloaded from the internet, free of charge at: **www.nhlbi.nih.gov/health/prof/blood/sickle/index.htm**

- American Academy of Pediatrics. (2002). Health Supervision for Children with Sickle Cell Disease. Pediatrics:109;526-535.

This technical report, developed by the American Academy of Pediatrics, outlines the care that a child who has sickle cell disease should receive. A full-text version of this report is available at: **www.aap.org/policy/re1011.html**

- The Sickle Cell Information Center.

This Web site provides sickle cell patient and professional educational materials, news, research updates, and world wide sickle cell resources. The site is managed by the Georgia Comprehensive Sickle Cell Center at Grady Health System in Atlanta, GA and can be found at: **www.scinfo.org**

- The National Newborn Screening and Genetics Resource Center (NNSGRC)

The NNSGRC provides information and resources in the area of newborn screening and genetics to benefit health professionals, the public health community, consumers, and government officials. The NNSGRC provides technical assistance to state newborn screening programs and gathers and compiles state-specific data from these programs as well. A newborn screening information report can be found at the NNSGRC Web site: **genes-r-us.uthscsa.edu/**

Endnotes

[1] National Institutes of Health. (2002). The management of sickle cell disease. NIH Publication No. 02-2117.

[2] American Academy of Pediatrics. (2002). Health supervision for children with sickle cell disease. Pediatrics;109:526-535

[3] Consensus Development Panel, National Institutes of Health (1987) Newborn screening for sickle cell disease and other hemoglobinopathies. JAMA; 258:1205-1209

[4] Pass KA, Lane PA, Fernhoff PM, et al. (2000) US newborn screening system guidelines II: follow-up of children, diagnosis, management, and evaluation. J Pediatr;137(suppl):S1-S46