



# **GUIDELINES FOR THE TREATMENT OF PEOPLE WITH SICKLE CELL DISEASE**

**Written by members of SCAC (the Sickle Cell Advisory Committee) of  
GENES (The Genetic Network of New York, Puerto Rico and the Virgin  
Islands) with the support from grants from HRSA**

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## FOREWORD

One of the primary concerns of the Sickle Cell Advisory Committee (SCAC) of the Genetic Network of New York, Puerto Rico and the Virgin Islands (GENES) has been the improvement of care for the sickle cell patient. This concern is particularly relevant because of the variety of settings in which these patients receive care and because of the impact that changes in the health care system has had on these settings. In line with the current national movement toward devising “practice guidelines” and “clinical pathways,” as well as initiatives already begun in other states such as Texas and Colorado, SCAC established a subcommittee in 1997. Its members were charged with writing clinical guidelines as a means of both assisting the practitioner who renders care to patients with sickle cell disease, and providing a means of assessing the adequacy of care. The following guidelines represent a consensus document by health care providers who have both expertise and experience in working with sickle cell patients, and includes significant consumer input. Whenever possible, recommendations are evidence-based, but it should be noted that sickle cell disease is extremely protean in causation, pathophysiology and presentation. In many instances rigorous scientific data do not exist for recommendations. A comprehensive list of references is provided, and usually when recommendations are based on established practice of qualified hematologists, rather than on extensive clinical trials, this fact is noted. We chose to use a dual format: a brief text followed by a schematic algorithm, with the assumption that this provides the reader the maximum clarity with the minimum time investment.

The essence of the message in this set of guidelines is as follows: The primary care physician, as the front line provider, must be well versed in issues related to screening/diagnosis, health maintenance, including prophylaxis, preventive care and anticipatory guidance; and must be cognizant of basic issues in differential diagnosis. Sickle cell disease involves multiple organ systems. This is understandable in a disease of the blood. Common symptoms, which in other patients might indicate common diseases, in the patient with sickle cell disease can indicate potentially serious complications, unique to the sickle cell patient. These complications must be suspected early. Prompt diagnosis followed by judicious treatment by the primary care physician, and the subspecialist when appropriate, can avert disaster. The value of “sickle cell centers” lies in the availability of medical and technical expertise in one location, with maximal accessibility. If the primary care physician has ready access to such a center, he or she can ensure that the patient receives optimal care.

### **History and Mission of SCAC**

SCAC, the Sickle Cell Advisory Committee, had its origin in the late 1970s as a conglomeration of sickle cell providers with a firm commitment to the care of patients with sickle cell disease. They had the vision to join forces for the accomplishment of mutual goals, and developed an initial mandate to help with the state-wide implementation of newborn screening follow-up. SCAC was conceived as a broad-based body, representative of both professionals who work with sickle cell patients, the patients themselves and their families. SCAC saw itself as of potential use to government bodies and to any organization with “sickle cell needs.” Although its original purpose was to offer assistance to genetic services at the state level, it received its current structure when GENES was identified as a region within the federally funded, public health-oriented, nationwide network of genetic services. GENES, the Genetic Network of New York,

Puerto Rico and the Virgin Islands, is funded as one of ten networks that comprised CORN, the Council of Regional Networks for Genetic Services. Note: CORN ceased to receive federal funding in 1999. Funding for GENES will continue only through the summer of 2002.

SCAC serves as an advisor to GENES and, through GENES, to the New York State Department of Health and many other entities nationally as well as internationally. It consists of representatives of most of the comprehensive sickle cell programs in the state, whether they receive federal, state or local funds. The professionals can be hematologists, pediatric hematologists, pediatricians, geneticists, internists, or other physicians; nurses or nurse practitioners; genetic counselors, social workers, health educators, laboratory technologists, or public health professionals. Of particular importance to SCAC is the Director of the NYS Newborn Screening Program and his staff. Essential components of SCAC's membership are patients who have sickle cell disease and their family members, and representatives from community organizations established to give assistance to patients with sickle cell disease.

SCAC has had major input into the state's implementation of newborn screening for sickle cell disease, in developing instruments to collect data pertaining to newborn screening, and in structuring evaluation criteria for statewide genetics grants as they pertain to services for patients with sickle cell disease.

SCAC sees its role as encompassing any and all issues concerning any facet of sickle cell disease, from medical to psycho-social, from the community to the legislature. Specifically, its concerns are education, newborn screening, patient care, outreach, lobbying, research, and advocacy. It serves as a forum for discussion of problems and developments in the field of sickle cell and is a major provider of education about sickle cell disease to medical professionals and the lay public. Members are from New York City, the greater metropolitan area and the larger upstate New York cities. SCAC functions through a general assembly and an executive committee consisting of the officers and the chairs of the subcommittees. There are three general and three executive meetings each year. SCAC also sponsors an annual symposium where nationally recognized experts in the comprehensive care of patients with sickle cell disease share new developments and where patients and their families bring the realities of living with sickle cell disease to the medical and public health professionals. SCAC is in the process of becoming incorporated as a non-profit organization and will continue as a vital entity for the foreseeable future.

## INTRODUCTION

Sickle cell disease is a term used for a group of conditions in which the pathology is due to the presence of hemoglobin S. Sickle cell anemia, or homozygous sickle cell disease, results from the inheritance of a sickle cell gene from both parents. Other genotypes of sickle cell disease result from the inheritance of one hemoglobin S and another abnormal hemoglobin such as C, causing SC disease, or a thalassemia gene causing  $S\beta^+$  or  $S\beta^0$  thalassemia. Sickle cell disease is characterized by continuous red blood cell hemolysis usually resulting in anemia. This varies from patient to patient from inconsequential to severe; causing the variable presentation of painful vaso-occlusive crises; the potential for serious infections in childhood; and acute complications involving any of the major organ systems, with progressive, irreversible organ damage. In sickle cell trait (the carrier state) there is always more normal (A) hemoglobin than S hemoglobin. Patients with sickle cell trait do not have symptoms from their sickle hemoglobin except under extraordinary conditions.

Eighty-five percent of people born with the disease now live to age 20, and most patients now survive at least until middle age. Patients are usually able to complete high school; many go on to college and graduate school; and all have the potential to lead productive lives. This greatly improved prognosis over the past generation is the result of newborn diagnosis and intervention, including the use of prophylactic penicillin from the age of three months, comprehensive health maintenance, and the immediate treatment of acute complications, in combination with several therapeutic advances.

Each patient with sickle cell disease needs a satisfactory “medical home” tailored to his or her individual needs. These needs can be met in a variety of ways, most of which are compatible with the current medical care system. Medical care is best provided in a comprehensive sickle cell program where patients receive primary and preventive care, comprehensive health maintenance, and therapy related to the acute and chronic manifestations of sickle cell disease. Hematology clinics with physicians knowledgeable about all aspects of sickle cell disease who can ensure that patients receive optimal primary care and timely specialty referrals are appropriate. Primary care physicians, either in solo practice or working in health maintenance organizations, with unimpeded access to all the services these patients need, can also provide quality care. Wherever the patient receives care, there must be a coordinated approach between the physician in charge of the case and other health care professionals needed at any point in time: specialist physicians (e.g. ophthalmologist, neurologist, orthopedist, nephrologist, pulmonologist), social workers for therapy or case work, genetic counselors, nurse clinicians, or other health care providers. The patient should be able to reach the primary physician promptly and, in an emergency as defined by his or her physician, to obtain care in an Emergency Department or Comprehensive Sickle Cell Program without prior approval. Emergency Departments should have unimpeded access to important aspects of the patient’s medical history, such as baseline laboratory values and occurrence of prior complications. Immediate access to this information would expedite emergency room assessments, tests and hospitalizations.

### **Purpose**

The purpose of these guidelines is to assist all programs that provide care for sickle cell patients to foster and implement a system of comprehensive care which enables:

- Primary care physicians, regardless of the milieu in which they practice, to utilize appropriate health care maintenance protocols for individuals of any age and ensure the optimal treatment of acute complications
- Primary care physicians less familiar with the disorder to determine when to consult with or refer to an expert
- Case managers and those who perform quality investigations, audits, etc., to assess the adequacy of care.

It must be emphasized that these guidelines do not replace on-going care by knowledgeable providers.

Comprehensive sickle cell care should provide or assure:

- Availability of comprehensive primary, secondary and preventive care
- Continuity of care including compliance with treatment and medication
- Compliance with a schedule of follow-up visits
- Availability of psychosocial support
- Availability of emergency care and 24 hour physician coverage
- Availability of consultation for proper treatment during emergency room visits, health maintenance visits, inpatient stays, and surgical and obstetrical needs. A “team approach” is optimal.

Comprehensive care should also provide patient support networks and current informational materials for new health care providers, teachers, employers, patients and their families.

The existence of such comprehensive services to date has resulted in:

- Decrease in cost by obviating unnecessary hospitalization
- Decrease in morbidity and mortality
- Reduced length of hospital stay
- More appropriate discharge planning
- Increased functional ability on the part of the patient, as well as improved quality of life
- Increase in patient/family satisfaction.

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## NEWBORN SCREENING

Newborn screening for sickle cell disease is an effective first step taken to reduce morbidity and mortality in individuals with the disease (SS disease, the classical sickle cell anemia, as well as sickle C disease, sickle  $\beta$ -thalassemia, and other less common variant sickle cell diseases). Every infant born in New York State is screened for sickle cell disorders and a number of other conditions. The hospital of birth and the physician of record are notified by the state newborn screening program about the birth of an affected baby. Any licensed NYS physician can obtain the screening result on a patient by contacting the state's 800 phone number: (800) 535-3079. Parents of children with a sickle cell disease should be contacted by their pediatrician or hospital of birth before the child reaches two months of age. This is so the test can be repeated in the state laboratory for verification of the initial result and so the physician can establish a definitive diagnosis through additional laboratory testing of the child and the parent(s). All laboratory tests must be performed in qualified state licensed laboratories, with specific competence in analysis of variant hemoglobins. Because of the high concentration of hemoglobin F in newborns, solubility tests, or sickle cell preparations (sodium metabisulfate) must not be used to determine hemoglobin S in early infancy. In any event, these tests should never be used as sole diagnostic laboratory procedures. A pediatric hematologist can be consulted in the diagnostic process.

If a child who is presumed to have sickle cell disease through newborn screening is not retested by four months of age, he or she should be started on penicillin VK (125 mg given orally twice a day) pending confirmation. Once the diagnosis is confirmed, the infant must receive care in an ongoing, comprehensive medical program. Treatment includes oral penicillin given twice a day to most children with sickle cell disease for prevention of overwhelming *Streptococcus pneumoniae* infection as well as pneumococcal vaccine from two months of age. The program should also include extensive parent education. The medical program should be staffed by health care professionals who are sensitive to the special needs of infants with sickle cell diseases, and are aware of their high risk for sepsis and complications such as acute splenic sequestration and acute chest syndrome. (See section on Routine Health Maintenance for further details.) The dramatic improvement in the life expectancy of children with sickle cell disease today over that of 30 years ago – an increase from 50% to 85% if the child receives good care – is largely due to newborn screening followed by comprehensive care from knowledgeable providers. If the child is under the care of a primary care pediatrician, rather than a designated sickle cell program, the physician should maintain contact with a pediatric hematologist or a Sickle Cell Center so that consults are readily available and hospitalization in a tertiary care facility possible without delay.

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## GENETIC TESTING AND COUNSELING

As sickle cell disease and thalassemia are autosomal recessive inherited conditions, genetic counseling is an important component of comprehensive care. Genetic counseling not only includes counseling on the basis of inheritance patterns, but also includes discussion of the origin and significance of various hemoglobin genes and future reproductive options.

When patients have a clear understanding of all aspects of their medical condition, they have the opportunity to make better decisions regarding medical treatment and family planning. Sensitive counseling and support can address psychosocial concerns regarding disease and trait status. It is generally accepted that patients make autonomous decisions in regard to their reproductive options. Every attempt is made to provide genetic counseling in a nondirective fashion.

Initial diagnosis of hemoglobin disease or trait status is of fundamental importance in genetic counseling. A CBC with manual differential, hemoglobin electrophoresis with fetal and A<sub>2</sub> quantitation, IEF or HPLC, as well as ferritin levels are usually done for a definitive diagnosis. The hemoglobin electrophoresis procedure will reliably diagnose most forms of sickle cell disease or trait conditions as well as other variant hemoglobin disease or trait conditions. Utilization of sickle prep and Sickledex® or other solubility tests in place of the electrophoresis will not accurately define hemoglobin status and will miss certain hemoglobin variants. These tests should **never** be used for diagnostic purposes. The only appropriate screening test for diagnosis is hemoglobin electrophoresis.

### **When is Genetic Counseling Provided?**

It is generally accepted that genetic counseling should be provided to the family at the time of the initial diagnosis of an S hemoglobinopathy in a child. Genetic counseling should be provided to the patient with disease or trait during adolescence and before each pregnancy. Genetic counseling should also be available at any other time requested by the family or at the discretion of the primary caregiver.

### **What Should be Included in a Genetic Counseling/Education Discussion?**

- A detailed family history with appropriate genetic consultation for any other concerns
- The function of normal hemoglobin
- The medical significance of abnormal hemoglobins, such as S, C or others as appropriate
- The inheritance pattern of variant hemoglobin types, including significant combinations of hemoglobin genes
- All reproductive options available, both preconception and prenatal
- The evolutionary response of genes in a population to environmental conditions (i.e., the concept of heterozygote advantage)
- A discussion of psychosocial aspects of disease or trait status
- Referral for hemoglobin electrophoresis testing for other family members with information on the limitations of sickle cell preparations and Sickledex® or other solubility tests
- Provision of literature in patient's primary language on above topics for patients and other family members
- A written description of genetic diagnosis, type of inheritance and reproductive risk

- Referral for additional counseling as needed or as per the family's or primary caregiver's request
- Genetic counseling is also provided to the patient who has been identified with a hemoglobinopathy during pregnancy. The patient is strongly encouraged to bring the biologic father in for testing.
- When a family at risk for having a child with sickle cell disease is counseled, they should be made aware of the advantage of cord blood storage from a normal or trait sibling to serve as a possible source of stem cells for the affected child. This procedure can be coordinated through a sickle cell center or program.

### **Who Provides Genetic Counseling?**

A board certified/eligible genetic counselor, trained single gene disorder counselor or health educator affiliated with a sickle cell/thalassemia center are the preferred providers of this service. A hematologist or medical geneticist should be consulted as needed.

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## SOCIAL WORK

Families of children, adolescents and adult patients with sickle cell disease can exhibit a variety of complex problems due, in part, to the chronicity of their disease and the recurrent episodes of their illness. The initial bio-psychosocial diagnostic interview is critical in identifying such issues as the underlying genetic guilt parents may carry, as well as unresolved issues about their own trait status and its implications for future childbearing. Coordination of services demands an assortment of skills and abilities that are unique to social work and are provided by trained, licensed, professional social workers. Social workers coordinate services for patients and families with sickle cell disease by managing the systems that impact on the family homeostasis and equilibrium.

The social worker will

- Address a range of needs a family may have (i.e., housing, insurance, employment, unemployment, substance abuse concerns and domestic violence, etc.).
- Serve as a mediator and vocational link between family systems and social systems.
- Make available resources in the community that can help patients to improve their overall quality of life.
- Link families via group process to help adjust to a new diagnosis and the frequent hospitalizations of patients.
- Play an integral part in the treatment process.
- Intervene with colleagues to further enhance the working relationship within the team.
- Help identify cultural belief systems, myths and superstitions that impact on medical intervention.
- Evaluate all questions of child abuse, neglect, or possible placement concerns.

Social work intervention is needed at each phase of the patient's and family's development regarding the manifestation of the disease process over time. Social workers help patients and families identify strengths that will enhance coping and adaptation to illness and improve familial harmony and quality of life.

Without social work serving as the "hub" of comprehensive care services and networking for patients and families, both quality of life and longevity are jeopardized. Social workers intervene to minimize the threat of family breakdown and disequilibrium.

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## NURSING CONCERNS

The nurse's role is pivotal to the comprehensive care of individuals with sickle cell disease. It centers around providing ongoing education about the disease, ensuring a system of preventive health management, recognition and management of acute illnesses, and the timely coordination and integration of subspecialty care. In addition, the nurse plays a central role in developmental and emotional anticipatory guidance and in the empowerment of the patient and family for their own advocacy.

### Nursing Responsibilities in Emergency Department/Inpatient Setting

#### Observation/History/Mental Status

- Observe patient's color – look for pallor, especially in young children. Note if it is of sudden onset accompanied by weakness, lethargy, headache, fainting or other inappropriate behavior. Observe sclera, check pupils, check for jaundice.
- Observe for respiratory symptoms and increased oxygen demands. Observe depth and quality of respirations. Check pulse oximetry. Note any acute chest pain, dyspnea or cough.
- Observe patient's disposition and signs and symptoms of pain, including splinting, grimacing, other facial expression, or lying in a rigid manner.
- Evaluate mental status with or without pain. Depression and suicidal ideation should be considered.
- Monitor vital signs. Indications of bacterial infection and overwhelming sepsis can be fever, tachycardia and hypotension.
- Assess hydration status.
- Obtain comprehensive nursing history including prescription medicines, alternative therapies and history of the current event, including any recent exposure to illness or infection. Note ambulatory status including limp with or without pain.
- All pubertal and prepubertal male patients - obtain history of priapism.

#### Physical assessment

- Auscultate chest – note breath sounds and the presence of heart murmurs.
- Palpate abdomen – check spleen and liver size and note any tenderness or increased pain.
- Check extremities for bone, joint, or soft tissue pain. Note presence of inflammatory process including heat, redness, tenderness and swelling. Assess level of pain and mental status.
- Assess for neurological deficit – weakness on one side of the body including facial drooping, slurred speech, unsteady gait, changes in vision, numbness or tingling of an extremity, and/or paralysis. Ask if any seizures were noted.
- BE CAREFUL TO DISTINGUISH BETWEEN SICKLE AND NON-SICKLE EPISODES.

#### Specific Interventions

- Administer prescribed medications.

- Administer pain medication promptly.
- Administer antibiotic after appropriate diagnostic work-up.
- Follow physicians' orders for diagnostic tests.
- Reevaluate every 15 to 30 minutes for change in status.
- Monitor intravenous infusion/transfusion.
- Ensure that the hematologist or primary care provider is notified.

### **Nursing responsibilities in Office/Clinic setting**

- Monitor vital signs.
- Monitor growth and development – note weight/height for age.
- Take diet and nutritional history, emphasizing the importance of fluid intake and adequate caloric intake.
- Take interval history including immunization status and any medication changes.
- Review patient and family knowledge of genetics and the availability of prenatal diagnosis when relevant. Educate about harvesting and storage of cord blood stem cells.
- Reinforce education regarding the disease process, recognition of illness symptoms, especially temperature and palpation of spleen, the importance of prompt medical intervention for fevers, home management of pain, and noting and avoiding precipitating factors for crises.
- Discuss age appropriate behaviors and developmental issues.
- Encourage participation in support groups
- Ensure continued hematology follow-up and multi-disciplinary management.

### **Telephone Triage**

This is pivotal to the early identification, prompt evaluation and effective treatment of sickle-related symptomatology and co-morbidities. Co-morbidities severely impact the well-being of these patients and usually result in major sickle-related complications. The unpredictable and intense nature of sickle cell pain cannot be overstressed. Patients and families calling should be educated to preface their comments with, "I have/my family member has sickle cell disease." It is very important for the triage nurse to inquire about pain.

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## ROUTINE HEALTH MAINTENANCE

It is now known that the median life span for individuals with sickle cell disease is 50 years for those with the SS genotype and even longer for other genotypes. More than 85% of children born with sickle cell disease will reach the age of 20. The general concepts of health maintenance and preventive care are as important to these patients as to any other group, but certain special precepts pertain.

### **Diet, nutrition and vitamin supplements**

Infants, unless they are breast fed, can be kept on iron fortified formula for the first year. The diet should be optimal at all ages. Multivitamins with maintenance iron are appropriate up to the age of 2 years, and even thereafter if the child's food intake is erratic or unbalanced. Folic acid (1 mg/day) is not essential for all patients, but is important if there is significant hemolysis. Growth of the child and adolescent should be carefully monitored. If there is significant lag, the patient must be assessed to rule out other causes of growth delay. In their absence, dietary supplements such as Ensure™ or Nutrament™ can be given. Peripubertal delay of both growth and sexual maturation of as much as 2 years is frequent in children with SS disease. It is important to reassure the patients and the teenager that there will be catch-up in both, so that adult size and development will be within normal limits. (See Growth and Development Section.) The government-issued food pyramid guidelines should be followed. In addition, adequate fluid intake is important.

Penicillin prophylaxis should be given to all patients with SS disease and  $S\beta^0$  thalassemia, as well as to those children with any type of sickle cell disease who have undergone splenectomy. Infants with  $S\beta^+$  thalassemia and SC disease may be given prophylactic penicillin at the discretion of the hematologist. The penicillin is started at 2 months of age at a dose of 125 mg bid, changed to 250 mg bid when the child reaches three years. When the child is one year old, the penicillin can be given in pill form by crushing the pills and mixing them with applesauce or syrup. Although the children whose spleens have been removed should remain on prophylaxis through adolescence, penicillin may be discontinued when the other patients reach 5 years of age at the discretion of the physician. Erythromycin at half the therapeutic dose bid is recommended if the child is allergic to penicillin. The recently released conjugated heptavalent pneumococcal vaccine should be given from the age of 2 months, and the 23 valent non-conjugated vaccine at 2 and 5 years of age.

### **Chronic medications**

Besides penicillin and folic acid discussed above, the most important sickle-related medications given chronically to patients with sickle cell disease are hydroxyurea and desferal. Hydroxyurea has proved effective in reducing the incidence and severity of pain episodes and acute chest syndrome in adults with SS disease. Since it has the potential for causing both hematologic and clinical side effects, the patient must be followed carefully, with clinical assessment as well as blood tests every two weeks.

When an individual is on a chronic transfusion regimen, ferritin must be measured periodically to identify the onset of iron overload. This usually begins after a year of therapy. Some hematologists advise that periodic liver biopsies provide a better indication of iron

accumulation.. Once there is evidence of significant iron in blood or liver, the child must be started on desferal delivered subcutaneously 5 to 7 times per week.

An important task of the primary care physician is to monitor compliance with chronic medications, constantly reinforcing their importance. The PCP must make sure that required testing is performed at necessary intervals, and that the test results are scrutinized.

### **Special considerations for the adolescent and adult**

Adolescents with sickle cell disease are now surviving far into adulthood. This has resulted in a need for transition programs to assist families and health care providers in the transition process from pediatric to adult medicine. Preparation for transition must begin early in adolescence. Issues associated with the transfer from a pediatric to an adult care setting are the adolescent maturity level and competence for self-management and the fears, beliefs and attitudes toward leaving pediatrics.

A transition focused intervention program that addresses the psychosocial and educational needs of adolescents with sickle cell disease should be made available. These programs should offer:

- Introduction to a culturally competent internist, and to a hematologist in the geographic area
- Provision of a complete medical history to be transferred with the patient. The records that should be included are EKG, echo, ophthalmology, audiology, pulmonary function, transcranial Doppler and other consultation reports.
- Adequate case management to navigate health insurance companies, the demands of multidisciplinary care and application for disability benefits
- Promotion of self-reliance, self-awareness and individualized management for health care needs
- Assistance to the patient in adjusting to employment and the reality of being an adult with a chronic condition.

Transition to adult hematology services for adolescents with sickle cell disease can begin at age 15 and is usually completed by age 21. The goal should include education about sickle cell disease and medical self-management so that the patients become more competent in interacting with the health care team.

Health maintenance for the adult and adolescent patient with sickle cell disease, as for any other patient, should include counseling on relevant issues such as pregnancy and contraception, avoidance of high risk sexual behavior, substance abuse and smoking. The age appropriate screening recommendations for the general public should be observed. No form of contraception has been specifically contraindicated for women with sickle cell, thus selection can fit the specific needs of the individual patient. It is also important to ensure that patients clearly understand their hemoglobin genotype and its implications for offspring. Patients should be encouraged to complete their education so they will get the skills necessary to compete successfully in the job market. The physician should advocate for the patient in the school or employment setting with reference, as needed, to Federal and State regulations concerning persons with disabilities.

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## RECOMMENDED OUTPATIENT FOLLOW-UP

AGE	REGULAR VISITS*	LAB TESTS*	IMMUNIZATIONS** IN ADDITION:	SCREENING PROCEDURES	OTHER SCREENING PROCEDURES
0-6 MONTHS	EVERY 2 MONTHS	CBC EACH VISIT	HEPTAVALENT CONJUGATED PNEUMOCOCCAL VACCINE AT 2 ,4, 6 MONTHS	HEARING, VISION, PPD**	
6 MONTHS – 2 YEARS	EVERY 3 MONTHS	URINE YEARLY CBC EACH VISIT IRON/TIBC ONCE	HEPTAVALENT CONJUGATED PNEUMOCOCCAL VACCINE BOOSTER AT 15 MONTHS, FLU VACCINE AS INDICATED	HEARING, VISION, PPD**	
2-5 YEARS	EVERY 6 MONTHS	FERRITIN*** OR IRON/TIBC ONCE URINE YEARLY BUN, CREATININE, LFT, CBC EACH VISIT	PNEUMOCOCCAL VACCINE 23 VALENT AT AGE 2, BOOSTER AGE 5, FLU VACCINE AS INDICATED	HEARING, VISION, PPD**	FROM 2 YEARS PERIODIC DENTAL EXAMS** ****
OVER 5 YEARS	EVERY 6-12 MONTHS	URINE YEARLY CBC EACH VISIT	FLU VACCINE AS INDICATED	HEARING, VISION, PPD**	RETINAL EXAM YEARLY FROM AGE 10 ****
ADOLESCENCE	YEARLY	BUN, CREATININE, LFT ONCE OR YEARLY, FERRITIN*** OR IRON/TIBC ONCE URINE YEARLY CBC EACH VISIT	FLU VACCINE AS INDICATED	HEARING, VISION, PPD**	RETINAL EXAM YEARLY ANNUAL PAP SMEAR FOR SEXUALLY ACTIVE GIRLS ****
ADULT	YEARLY	BUN, CREATININE, LFT YEARLY, OTHER TESTS**, URINE YEARLY CBC EACH VISIT	FLU VACCINE AS INDICATED	HEARING, VISION, PPD**	RETINAL EXAM YEARLY ANNUAL PAP SMEAR, MAMMOGRAM, PROSTATE EXAM** ****

\* These recommendations include a complete history, physical exam and growth assessment. More frequent visits and laboratory work will be required for management of chronic and intercurrent problems.

\*\* Follow standard practice

\*\*\* Iron studies must be done more frequently if child is on chronic transfusions to monitor for iron overload.

\*\*\*\* Transcranial Doppler examinations, cranial MRIs, cardiac evaluations, pulmonary function tests, psychological assessment, orthopedic evaluation and other special studies will be needed in selected cases, either for screening or on clinical indications. Since the need, diagnostic techniques used and interpretation of results must be individualized, these tests should be ordered with input from the sickle cell hematologist or other expert.

## GROWTH AND DEVELOPMENT

Children with SC disease or  $S\beta^+$  thalassemia usually grow normally. Children with SS disease and  $S\beta^0$  thalassemia are frequently growth delayed. Delay of growth and sexual maturation usually becomes significant immediately prepubertally, and may cause as much as a two-year lag. There will be catch-up growth and maturation, so that by the time the child reaches his or her twenties, he or she will have caught up with peers. If the delay is more than anticipated, or if the child reaches a plateau in growth/maturation, a work-up and/or nutrition/ endocrinology consultation is indicated. In the absence of causes other than sickle cell be sure to reassure both the family and the child that the growth lag is temporary.

Even if the child with sickle cell disease has a good appetite, it is still not always possible for him to accommodate the extra demands of his cardiovascular and hematopoietic systems. The child should be given a balanced diet, supplemented with vitamins and folic acid as needed. The child under two should be given maintenance iron to supply enough for growth unless he has already been transfused. If the young sickle cell child has a poor appetite, as for any child, he should be tested for iron deficiency, and iron can be supplied in therapeutic amounts, if indicated.

Unless there is CNS involvement, present in a minority of cases (See CVA), the child with sickle cell disease has mental development within the normal range. If there is a fall-off from expected milestones or in school performance, hematological, psychometric and neurological evaluations should be obtained.

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## EMERGENCY DEPARTMENT (ED)

Often the portal of entry to the hospital, or to medical care in general for sickle cell patients, is the emergency department. An appropriate approach to the patients, sensitivity to their symptoms and complaints, and knowledge of the various manifestations of sickle cell disease is crucial. Inexperienced hospital staff may fear that patients with sickle cell disease misuse the emergency department and are participating in drug seeking behavior. It must be emphasized that only a very small percentage of sickle cell patients misuse emergency department services. This small percentage could be reduced further if these patients receive care and are referred to a comprehensive sickle cell program for periodic consultation or for assistance in managing complications. It is important that the medical staff and all other personnel remain sensitive to the patients' complaints and treat all patients in a courteous, compassionate and expeditious manner.

Sickle cell disease is known to have many clinical manifestations caused by the abnormally shaped red cells and the micro-occlusions they cause. Differences among the various genotypes of sickle cell disease as well as other factors that may influence the phenotypic character of the disease, make it important that each patient be treated individually. **When patients with sickle cell disease come to the emergency department they should be triaged rapidly, and the physician responsible should be notified of their presence as soon as possible.** The most frequent presenting complaint of patients with sickle cell disease is pain and it is imperative that this particular problem be addressed appropriately. Fever is a frequent presenting complaint of children with sickle cell disease and represents a true emergency because it can herald the onset of overwhelming sepsis. Patients with sickle cell disease, especially those less than 5 years of age, are at an increased risk of *S. pneumoniae* and *H. influenza* infection because of their dysfunctional spleens. In addition, an enlarged spleen may indicate the onset of acute splenic sequestration crisis (see guideline). Other common presenting complaints and findings are respiratory distress, neurological symptoms, lethargy, significant pallor, weakness and acute anemia and urinary findings. Because all patients with the same genotype (e.g. Hb SS) do not have the same clinical course, it is imperative that the patient's hematologist and primary care physician be contacted as soon as possible. These physicians will know the patient's pertinent past medical history, as well as the treatment to which the patient best responds.

Refer to algorithms for specific complications when applicable. Discussion of "limp," "pain," and "infection" follow, since they encompass presenting symptoms frequently seen in the ED.

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## PAIN

Pain is the manifestation of sickle cell disease most frequently seen by the primary care provider, and, on average, the most distressing to the largest number of patients with sickle cell syndromes. Sickle cell pain can begin in infancy and last through the patient's lifetime. Many barriers exist in the treatment of sickle cell pain including failure to believe the patient's report of pain intensity and the amount of medication required, fear of addiction, differences in the sociocultural background between patients and health care providers, and lack of continuity of care. However, the knowledgeable practitioner can manage sickle cell pain effectively.

Sickle cell pain can be acute, chronic or combined in nature, and can be caused or complicated by a variety of mechanisms related directly or indirectly to sickling. It can be intensified by psychosocial and cultural factors. Pain episodes vary in intensity and frequency among individuals, and in the same individual over time. It is important to remember that not all pain in the sickle cell patient is related to sickle cell disease. Therefore it is important to carefully determine the cause of the pain and to treat accordingly.

Major recommendations for the management of pain can be summarized as follows:

- Pain management should be prompt and aggressive.
- Severe pain is a medical emergency and should be treated accordingly.
- Pain should be quantitated in adults and children, using a validated pain scale.
- Analgesic use should be liberal, but tailored to the individual patient.
- Mild to moderate pain is usually controlled with acetaminophen or NSAIDs. If pain persists or escalates, opioids should be added.
- Adjunct methods such as acupuncture and psychological/behavioral methods can be utilized.
- Short duration pain can be controlled by opioids with short duration of action. If pain takes several days to resolve, a sustained release compound may be appropriate. For the hospitalized patient, consultation with the pain service is desirable.
- Meperidine use should be limited and should be avoided if it is anticipated that its use will be frequent or prolonged.
- When a patient is discharged from the in-patient service or from the emergency department after treatment for a pain episode, he or she should be given enough equianalgesic doses of an oral opioid to last until the follow-up visit a few days later.
- If the patient has continuous follow-up care in a facility with knowledgeable providers, the number of hospitalizations can be minimized.
- Opioid tolerance and physical dependence can occur with lengthy treatment; this is not addiction. Addiction is psychological dependence characterized by continued craving for an opioid for other than pain relief. Addiction is rare in patients under proper care.
- Older children and adults with severe recurrent pain may be candidates for hydroxyurea, given daily under the careful supervision of a hematologist, internist or pediatrician thoroughly familiar with this form of treatment. Hydroxyurea can lessen the severity and frequency of pain episodes in many patients with the SS genotype. The study of its use in the infant and young child has been limited.

The American Pain Society has recently published a monograph on the management of pain in sickle cell disease, which includes these recommendations, among others. The reader is urged to consult this as well as the other references noted below.

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## INFECTION, SEPSIS AND MENINGITIS

Serious bacterial infections are a major cause of morbidity and mortality in patients with sickle cell disease. Severe, overwhelming septicemia/meningitis due to *S. pneumoniae* is the most common cause of death during early childhood. Enteric organisms emerge as important pathogens in older patients. Infections also may enhance susceptibility toward vaso-occlusive complications. Prevention and early aggressive treatment of infection are critical in the management of patients with sickle cell disease.

Children with SS disease have a normal antibody response to vaccines and should receive all immunizations recommended by the American Academy of Pediatrics and the Public Health Service. In addition, children should receive the newly available heptavalent conjugated pneumococcal vaccine (Prevnar-Wyeth-Ayerst) at 2, 4, and 6 months, and booster at 15 months, as well as the 23 valent pneumococcal vaccine at 2 and 5 years. Adults who have no documented history of receiving pneumococcal vaccine should be immunized. Prophylactic penicillin is so effective in reducing the number of life-threatening episodes of pneumococcal sepsis in children with SS disease under age 5 that most states screen newborns for the disease so that affected children can be placed on the drug by 2 or 3 months of age. (See Newborn Screening and Health Maintenance Sections.)

Prophylaxis should be given to children with SS disease and S $\beta^{\circ}$  thalassemia starting at 2 to 3 months of age and continuing until at least age 5 years. Use of penicillin prophylaxis in SC disease is controversial. Although children with sickle cell disease of any type, and at any age can show increased susceptibility to sepsis, prophylaxis in older children has not been shown to be beneficial and may be unnecessary once pneumococcal immunizations are complete and antibody titers are protective. Compliance requires intensive education of the family. The emergence of penicillin- and cephalosporin-resistant *S. pneumoniae* is a serious evolving problem in many communities and may ultimately reduce the effectiveness of the established prophylactic regimen. At present, however, the most effective approach is a combination of traditional pneumococcal vaccinations and regular penicillin prophylaxis.

Fever in a child younger than age 5 years with SS disease often indicates life-threatening bacterial infection. Children with sickle cell disease and septicemia generally have fever greater than 102°F (38.9°C), but temperatures below 102°F may also be seen, especially early in the clinical course. In febrile children with sickle cell disease, administration of IV/parenteral antibiotics should occur promptly, even for minimal clinical indications such as significant fever, chills, etc. The patient should be evaluated for causes of fever such as otitis media, acute chest syndrome, or urinary tract infections. Chest x-ray, blood, urine, and throat cultures should be obtained promptly. Lumbar puncture should be performed even if there are only minimal indications of meningitis. An antibiotic effective against *S. pneumoniae* and *H. influenzae* should be administered, preferably intravenously, even before lab results are obtained. Because penicillin- and cephalosporin-resistant *S. pneumoniae* are now identified in many regions of the country, antibiotics such as vancomycin may be added to the typical empiric therapeutic regimen. Physicians should consider the susceptibility patterns of the local flora when selecting empiric therapy. The choice of subsequent antibiotics can be guided by results of cultures and clinical course.

Practice varies widely on indications for admitting febrile sickle cell disease patients to the hospital. There is, however, consensus that all patients with any of the following be admitted for inpatient treatment:

- Temperature greater than 40°C (≥104°F)
- Seriously ill appearance
- Hypotension
- Poor perfusion, dehydration, poor fluid intake
- Pulmonary infiltrate
- Corrected white blood count greater than 30,000/mm<sub>3</sub> or less than 5,000/mm<sub>3</sub>
- Platelet count less than 100,000/mm<sub>3</sub>
- Hemoglobin less than 5 gm/dl
- History of *S. pneumoniae* sepsis.

Several centers with expertise in treating large numbers of patients with sickle cell disease in an ambulatory setting have successfully used long-acting parenteral cephalosporins (e.g., ceftriaxone sodium) to treat febrile children as outpatients with daily follow-up. This approach is appropriate only when the following conditions apply:

- The patient is clinically at low risk for sepsis (i.e., none of the factors listed above is present)
- The patient, family, and clinic are capable of impeccable follow-up, (i.e. have phone and live near the health care facility) and the patient has immediate emergency access to the hospital
- A successful follow-up program has been established.

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## LIMP

This algorithm, like that for pain, is based on presenting symptoms, rather than an organ system. Since “limp” is often the presenting symptom in a child, particularly if he or she is pre-verbal, and can result from a variety of causes, of differing severity, it is important for the physician to plan a course of action dependent on specific physical findings. The initial and essential distinction should be between pain and neurologic causes as the explanation for a gait abnormality.

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## OSTEOMYELITIS

Infections are a major cause of morbidity and mortality for patients with sickle cell disease. Bacterial infections are the major cause of death in children during the first five years of life. There is an increased incidence of infections of the bones and joints in patients with sickle cell disease. Pain in the bones, joints and back is common in patients with sickle cell syndromes. Pain associated with a painful crisis is usually diffuse, however it can be localized. Because patients with sickle cell syndromes have an increased incidence of osteomyelitis, differentiating this from the usual pain crisis is important. There are very significant therapeutic and prognostic implications. Osteomyelitis should be considered in any patient with sickle cell disease who has tenderness, swelling, warmth, erythema, or other signs of infection. Systemic symptoms may include fever, weight loss, and recurrent pain episodes. Leukocytosis with left shift and elevated ESR are also common. Plain X-ray films are usually negative for the first week or 10 days except for soft tissue swelling, but can show destruction and new bone formation after that time. Bone biopsy/aspirations and cultures are usually diagnostic and are the procedures of choice if osteomyelitis is suspected. Bone scan with gallium follow-up or MRI can help distinguish an infectious process from that of an infarction.

Admission to the hospital is indicated for diagnosis and therapy. If the patient is febrile, intravenous antibiotics should be started to cover for salmonella, staphylococci, and enteric gram-negative organisms as well as *S. pneumoniae* in the infant, preferably after cultures of blood and area of inflammation have been obtained. Early orthopedic involvement in patient management is always warranted. Duration of intravenous antibiotic therapy and hospitalization is case dependent, but the usual course of treatment is at least 6-8 weeks if a diagnosis of osteomyelitis is confirmed.

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## **SPLENIC DYSFUNCTION AND ACUTE SPLENIC SEQUESTRATION**

Splenic dysfunction in sickle cell disease is the consequence of repeated infarctions and subsequent fibrosis of the spleen. Infants and young children with SS disease whose spleens have not yet undergone fibrosis, as well as a minority of older individuals with SS disease, and patients with other forms of sickle cell disease (e.g. SC and S $\beta^+$  thalassemia) can retain enlarged spleens into adult life. Patients with sickle cell disease may develop sudden intrasplenic pooling of large amounts of blood, a condition known as acute splenic sequestration crisis (ASSC). In SS disease, these events can occur as early as 2 months of age, but are unusual after the age of 3 years. In severe cases the spleen becomes enormous, filling the abdomen, and often extending into the pelvis. Clinical signs can be pallor, sudden weakness, tachycardia, tachypnea, and abdominal fullness. Because the anemia and hypovolemia can be profound, ASSC must be recognized and treated with dispatch to prevent shock and death.

Treatment of acute splenic sequestration is directed toward the prompt correction of hypovolemia with plasma expanders and urgent red blood cell transfusion. A dramatic regression of splenomegaly and rise in hemoglobin level can occur a short time after transfusion. Although blood transfusion is usually required, care should be taken not to over transfuse.

Early diagnosis of sickle cell disease permits training of patients to palpate their infants' abdomens to determine the size of the spleen. Parents must be instructed to seek immediate medical attention if they notice increased pallor, lethargy, abdominal pain or enlargement, or rapid splenic enlargement. Educating parents is an essential component of newborn screening follow-up and has resulted in reduced mortality from splenic sequestration.

### **Chronic Management**

Splenic sequestration crises can recur, and each event is a potential emergency. The only permanent cure is splenectomy, a procedure ideally performed after the age of 2 years. If the first episode occurs before the age of 2 years, one option is to administer monthly transfusions to lessen the chance of recurrence, and, with the family's concurrence, perform surgery after the child reaches 2 years and has received a course of heptavalent pneumococcal vaccine plus at least one dose of 23 valent pneumococcal vaccine.

### **Chronic Hypersplenism**

Occasionally a child with sickle cell disease will develop a chronically enlarged spleen, accompanied by a fall in the baseline level of hemoglobin, a greatly increased reticulocytosis, and frequently, a concurrent thrombocytopenia. This is evidence of a hypersplenic state. If the rate of hemolysis is severe, the child may require treatment by splenectomy. As with chronic management of ASSC, the decision regarding surgery should be made by the hematologist in conjunction with the parent and the pediatric surgeon.

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## ACUTE ANEMIA

Chronic anemia is characteristic of homozygous SS disease or  $S\beta^0$  thalassemia. Patients with SC disease or  $S\beta^+$  thalassemia usually have hemoglobin in the normal or low normal range.

Acute anemia is usually triggered by suppression of the bone marrow (viral or other infections), pooling of blood in the spleen or liver (sequestration), or increased intravascular hemolysis (hyperhemolytic crisis, DIC, etc.). It usually presents with acute onset of weakness, lethargy, pallor, breathlessness, palpitations, abdominal pain, and occasionally increased jaundice. Sickle cell patients are susceptible to any of the causes of anemia seen in other patients such as blood loss (e.g. epistaxis, meno-metrorrhagia, intestinal bleeding, etc.) or other causes of hemolysis (e.g. G6PD deficiency). Clinical findings of acute anemia may include tachycardia, tachypnea, pallor, jaundice, suddenly enlarged spleen/liver,  $S_3$  gallop, and/or congestive cardiac failure.

Because the red blood cell life span is shortened in sickle cell disease, even transient suppression of erythropoiesis can result in severe anemia. These episodes are called transient aplastic crises. The large majority of episodes of severe reticulocytopenia are due to infection by parvovirus B-19, which is also the cause of erythema infectiosum (fifth disease). Parvovirus B-19 is contagious; patients with aplastic crisis should be isolated from other individuals with sickle cell disease, immunosuppression and/or pregnancy.

Essential laboratory results of hemoglobin, hematocrit, reticulocyte count, and bilirubin, must be compared with baseline values. Treatment decisions should be made based on percentage of fall from baseline. In general, a fall of approximately 25-30% below baseline requires intervention, but decisions must be individualized according to the patients' clinical status and the circumstances surrounding the event.

Failure to correct a worsening anemia may result in heart failure and death. The patient must be closely monitored with carefully spaced CBCs, whether or not transfusions are given.

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## CHEST PAIN AND ACUTE CHEST SYNDROME (ACS)

Acute chest syndrome, a term used to describe new pulmonary findings on X-ray in individuals with sickle cell disease, is a leading cause of death and morbidity. Patients with ACS can have a fulminating clinical course, and any patient with complaints of chest pain, cough or respiratory difficulty should be seen immediately and carefully evaluated.

The common causes of chest pain are infarction of bones of the thoracic cage and/or acute pulmonary disease. Patients with rib or vertebral infarction are at risk for acute pulmonary disease due to hypoventilation due to splinting or narcotic analgesia or fat embolism from infarcted bone marrow. Infectious agents associated with ACS include viruses and atypical bacteria (*Chlamydia* and *Mycoplasma*) in addition to *S. pneumoniae* and other bacteria.

Common symptoms are pain, cough, fever and, occasionally, abdominal pain. Signs include tachypnea and shallow respirations. Auscultation of the chest may be normal, or subtle variations in aeration may be present early; ultimately most patients develop rales and other signs of consolidation. Palpation of the chest should be done to identify rib and/or vertebral infarction sometimes associated with swelling, warmth and erythema.

Laboratory findings include an X-ray of the chest which shows a new infiltrate (may be normal early in ACS). A hemoglobin drop is commonly seen in ACS. Erythroblastosis and thrombocytopenia are especially common in pulmonary fat embolism. Pulse oximetry should be performed routinely. Arterial blood gases, blood cultures, mycoplasma titers, typing and antibody screen should be performed selectively.

Treatment should include:

- A consultation with a hematologist early in patient's course
- Analgesics orally if pain is mild and parenterally for moderate to severe pain with attention to sedative effects
- Hydration with maintenance fluids - avoid over-hydration
- Incentive spirometry
- Pulse oximetry and oxygen as needed
- Antibiotics to include coverage with macrolides
- Transfusion for worsening respiratory distress, severe anemia or hypoxemia.

Mortality due to ACS is approximately 2%. Patients may develop progressive respiratory failure and an adult respiratory distress syndrome. Recurrent episodes of ACS are associated with chronic sickle cell lung disease in adults, which is associated with substantial morbidity and a 25% mortality rate.

Patients with recurrent ACS should have formal pulmonary function testing. Severely affected patients and those who have had recurrent ACS should be evaluated by the hematologist for institution of hydroxyurea therapy or a chronic transfusion regimen. Hydroxyurea requires close monitoring but can be effective in preventing severe or recurrent ACS.

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## **OBSTRUCTIVE SLEEP APNEA (OSA) DUE TO TONSILLO-ADENOIDAL HYPERTROPHY**

Obstructive sleep apnea (OSA) due to tonsillo-adenoidal hypertrophy is increasingly appreciated as a frequent cause of morbidity in the general population. The diagnosis is particularly pertinent in individuals with sickle cell disease, as periods of apnea with arterial oxygen desaturation and hypercapnia will potentially promote sickling and may put patients at risk for vaso-occlusive episodes or chronic organ damage.

Patients' families should be asked routinely if the patient snores. If so, a history of ineffective breathing, cessation of breathing, often with arousal from sleep, and daytime somnolence add to concern. History of tonsillitis and otitis media with effusion and especially with hearing loss are important. "Kissing" tonsils and adenoidal facies are typical but not always present.

An elevated plasma CO<sub>2</sub> suggests chronic hypoventilation. Arterial blood gases, especially if obtained while sleeping, can document hypoventilation and hypoxemia. A lateral neck X-ray may show a narrowed airway. Echocardiography and EKG should be performed to detect pulmonary hypertension. Finally, respiromnography can provide objective confirmation of severity by documenting apnea, hypopnea, paradoxical breathing, desaturation and heart rate changes.

Mild to moderate obstruction may benefit from a brief course of steroids, but children with persistent or severe obstruction require tonsillo-adenoidectomy (T & A). T & A is a surgical procedure with significant potential anesthetic/operative risk to the patient with sickle cell disease; patients should be prepared appropriately under supervision of a hematologist and frequently a pulmonologist, and the surgeon and anesthesiologist should be familiar with perioperative management of individuals with sickle cell disease. Preoperative transfusion is generally recommended for children with sickle cell disease requiring T & A.

Even in normal children, untreated OSA can lead to neurodevelopmental problems, failure to thrive, pulmonary hypertension, and even cor pulmonale. Children with sickle cell disease are at additional risk due to the potential of arterial desaturation precipitating a vaso-occlusive crisis; there is also a reported association of OSA and stroke in a child with sickle cell disease. Follow-up should be done with care, since signs and symptoms can recur.

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## CEREBROVASCULAR ACCIDENT (CVA)

Individuals with sickle cell disease are at risk for CVA at a rate of approximately of 0.5% per year. Seventy to ninety percent of these CVAs are due to cerebrovascular disease of the middle caliber cerebral vessels, with intimal hyperplasia causing luminal narrowing and distal cerebral insufficiency. Vascular damage continues, aneurysms develop, and intracranial hemorrhage is seen in adults with sickle cell disease, whereas ischemic strokes are more common in children. Although most strokes are of sudden onset, transient ischemic attacks (TIAs) can occur, often as a prelude to a complete stroke. While mortality is unusual from a first ischemic stroke, morbidity may be substantial, with severe motor and neuropsychological deficits. Intracranial hemorrhage in sickle cell patients carries a 25% mortality. Approximately 15% of children with sickle cell disease may have abnormalities on MRI suggestive of infarction without having overt neurological deficits. These “silent infarcts” are associated with specific neuropsychological deficits and an increased stroke risk.

Children with ischemic stroke most commonly present with sudden onset of numbness or weakness of an arm and or leg on one side of the body. Children are most susceptible to stroke between the ages of 2 and 10. If the dominant hemisphere is affected, aphasia maybe a presenting symptom. Occasionally convulsions are associated with a first episode of stroke and may also be seen post-stroke. Headache and obtundation are common presenting features of intracranial bleeding. Headache is a common problem for patients with sickle cell disease and because of the risk for neurological events it requires careful evaluation, usually with the assistance of a neurologist.

Individuals with sickle cell disease are at increased risk for meningitis, especially due to *S. pneumoniae*. Although most infected patients will have headache and stiff neck, in some sickle cell patients hyperpyrexia will be the only early manifestation of meningitis. A history of meningitis has been associated with increased risk of subsequent stroke.

Most individuals with sickle cell disease and stroke have hemiparesis and hyperreflexia on one side of the body. Sometimes at the first presentation of stroke more subtle neurological findings are present on the contralateral side due to previous subclinical cerebrovascular events.

There are no specific laboratory findings in individuals with sickle cell disease, although a more profound anemia, high white cell count, low fetal hemoglobin level, and recent acute chest syndromes have been associated with stroke risk. A CAT scan or MRI should be done urgently to rule out intracranial hemorrhage, which may require surgical intervention. MRI is more sensitive for picking up ischemic lesions than CAT scan, and if not done initially should be performed at some point to establish the extent of brain injury. Patients with meningeal signs and no evidence of increased intracranial pressure should have a lumbar puncture performed to look for meningitis. Transcranial Doppler ultrasonography, which identifies high blood flow velocity in the cerebral vessels of the circle of Willis, has been shown to be predictive of a first stroke in children with sickle cell disease and is a valuable screening tool.

An individual suspected of having a CVA should be hospitalized. If initial findings suggest intracranial hemorrhage, urgent neurosurgical consultation is required. For patients with a non-

hemorrhagic stroke, transfusion (generally exchange transfusion) should be given promptly. Transfusion is often followed by some recovery from neurological deficits. The goal of transfusion should be to lower the percent of hemoglobin S to less than 30%, and continuation of a chronic transfusion regimen to maintain this level of sickle hemoglobin is recommended to substantially reduce the likelihood of stroke recurrence (See transfusion). Chronic transfusion therapy has also been shown to substantially reduce the risk of first stroke in children with abnormal TCD.

In many individuals with sickle cell disease and stroke, prominent motor deficits and neuropsychological impairment persist, although recovery can occur over several months after the stroke. If chronic transfusion is not given there is a 47-90% recurrence rate, often with additional neurological impairment; ultimately death will occur in 25% of patients. Chronic transfusion therapy reduces the risk of recurrent stroke to less than 10%. Unfortunately, attempts to stop transfusion therapy even after several years often result in stroke recurrence and thus indefinitely prolonged transfusion therapy with its attendant need for iron chelation therapy is the rule. Recently a few patients have been managed with hydroxyurea and phlebotomy after a period of aggressive transfusion followed by a modified transfusion regimen to allow sickle hemoglobin to increase to 50-60%.

Patients receiving a chronic transfusion regimen need attention to optimizing the transfusion product (i.e., extended cross matching, white cell filtration, sometimes erythrocytapheresis). They also need monitoring for iron accumulation and must be started on chelation when ferritin levels and/or liver biopsy indicate significant amounts of iron. Once chelation has begun, the patient and family must be motivated to follow the prescribed regimen under careful scrutiny. Frequent testing will ensure appropriate therapeutic effect and avoid toxicity. Clearly, all chronic transfusion patients need to be managed directly by a pediatric hematologist with expertise in sickle cell disease and blood banking.

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## TRANSFUSION THERAPY

Transfusion therapy is not without risks. The most common are iron overload, alloimmunization and transmission of infections such as hepatitis or HIV. Since patients with sickle cell disease may require multiple transfusions over the course of their lives, the risks are multiplied, and except in acute emergencies, transfusions should only be given in consultation with a hematologist. Transfusion is not indicated in chronic, steady-state anemia, uncomplicated acute painful crisis, infection, uncomplicated pregnancy, or avascular necrosis.

Initial characterization of a patient's red blood cell antigen (phenotyping) is advisable at an early age or when first red cell antibodies have developed. Select donor blood to closely match the patient's phenotype. Extended cross matching for minor antigens is desirable. The patient's transfusion history should be checked for previous evidence of alloimmunization, as antibody titers may be undetectable months to years after the antibody challenge. Leukocyte-depleted PRBCs, preferably prefiltered blood and blood product should be used. Fresh blood less than 5-7 days old must be used. Use sickle cell negative blood to facilitate proper monitoring of post transfusion level of hemoglobin S through hemoglobin electrophoresis. Monitor outcome of transfusion therapy by measuring hemoglobin/hematocrit.

### Type of transfusion

- Simple: for severe anemia (<5g/dl); aplastic crisis, sequestration crisis, though the decision depends on the patient's clinical status, hemoglobin and hematocrit and the reticulocyte count, or prior to surgery when general anesthesia is anticipated. Volume of PRBC to be transfused should be adjusted to the pre-transfusion hemoglobin level to avoid cardiac overload.
- Chronic transfusion: for stroke prevention, to achieve a S hemoglobin level < 30%; chronic leg ulcers when local measures are unsuccessful; frequent priapism (for prolonged cases lasting more than 6-12 hours, consider a single volume exchange).
- Exchange transfusion, partial exchange transfusion or erythrocytapheresis (automated exchange) in specific cases, and, when appropriate, for acute chest syndrome and cerebral vascular accident.
- Automated exchange transfusion improves outcome in shorter time and has been proven to decrease the level of iron deposit

**Post transfusion (simple, chronic or exchange) hemoglobin level should never exceed 11 grams.**

The clinician should be aware that iron overload and consequent cardiac and other complications can occur after multiple transfusions. Periodic assessment of iron stores and prompt attention to any abnormalities noted are imperative. Most of these patients will require chelation therapy, which is given parenterally on a daily basis.

Autologous transfusion is not recommended.

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## SURGERY AND ANESTHESIA

Patients with sickle cell disease who undergo surgery have an increased risk of peri-operative complications and ambulatory surgery is usually not advised. Careful preoperative preparation, including CBC and reticulocyte count, urinalysis and PT and PTT, of the patient by a team consisting of a surgeon, hematologist and anesthesiologist will minimize or eliminate these complications. Patients with organ damage and/or coexistent disease must be identified because they are at increased risk for perioperative complications.

Surgical procedures that have an increased probability of ischemia or hypoxia deserve special attention. These include cardiothoracic surgery, techniques associated with hypotension, hypothermia, hyperventilation, and vascular surgery. Laparoscopic surgery appears to lower the postoperative complications of sickle cell disease and should be used in appropriate settings.

All patients should be evaluated by the anesthesiologist the day before surgery. Patients requiring general anesthesia should receive maintenance fluids at least 12 hours before surgery with strict attention paid to urinary output and weight. Transfusion is necessary only to raise the hemoglobin to 10-11 gm/dl. It is not necessary to lower the percentage of S hemoglobin a fixed amount by exchange transfusion. Patients with a history of pulmonary or CNS disease, recurrent hospitalization, and/or those who have been previously heavily transfused are at high risk for perioperative complications, especially ASC and vaso-occlusive events. A physical examination and chart review should be supplemented by the following tests:

- Arterial oxygen pressure or oxygen saturation measured by pulse oximetry
- Pulmonary function tests with bronchodilator response analysis regardless of a history of acute chest syndrome, asthma, or other pulmonary complications
- Echocardiogram
- Renal and liver function

Preoperative assessment of the patient should include signs of vaso-occlusion, fever, infection and dehydration. The laboratory and physical examination results should be reviewed to identify abnormalities in the heart, liver, kidneys, brain and lungs. The use of incentive spirometry prior to surgery should be encouraged. Careful post operative monitoring and management, including incentive spirometry, is essential to lessen the incidence of ACS, CVA and acute pain episodes.

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## HEART DISEASE

Cardiovascular manifestations in sickle cell disease occur because of chronic anemia, pulmonary arterial occlusion leading to *cor pulmonale* and myocardial damage resulting from small infarcts and iron deposition. Children and adolescents with SS disease or  $S\beta^0$  thalassemia and hemoglobin levels in the range of 6-8 gm/dl increase resting cardiac output 50% to meet the need for oxygen delivery to the tissues. Cardiomegaly is the rule in SS and  $S\beta^0$  sickle cell disease, and is seen in most children in the first five years. There is significant increase in left atrial and left ventricular dimensions. In adults, left ventricular hypertrophy (LVH), is constant and right ventricular hypertrophy (RVH) common. Cardiac output is elevated, and cardiac function may be abnormal on exercise. Congenital heart disease and lesions secondary to rheumatic fever, Kawasaki syndromes, and other illnesses that occur in childhood can be co-morbid conditions. In the adult, myocardial infarction and angina can also be seen.

### Symptoms and Signs

- Exercise intolerance (depends on hematocrit)
- Cardiac systolic flow murmurs (diastolic murmurs are unusual)
- Cardiomegaly with left ventricular hypertrophy
- Pulmonary hypertension and *cor pulmonale* after recurrent acute chest syndrome.
- Abnormalities are more severe with lower hemoglobins as in SS and  $S\beta^0$  thalassemia and less in patients with  $S\beta^+$  thalassemia and SC disease.
- Congestive heart failure is rarely seen except in the case of sudden and marked decrease in hemoglobin concentration.
- Many adults have concomitant hypertension and valvular disease, including mitral valve prolapse. Renal disease and pulmonary hypertension secondary to sickle vasculopathy in the lungs can further compromise cardiac function.
- Myocardial infarction is infrequent in adult patients with SS disease. Coronary artery anatomy in these patients is remarkable for the absence of significant arteriosclerosis.

### Management

- Patients should have baseline cardiac screening to assess status. Follow-up should be individualized.
- Physical activities are not usually contraindicated. Patients, both children and adults, should be allowed to set their own limits.
- Exercise can be performed but not to the point of exhaustion, and should be avoided under certain conditions such as cold weather or high altitude.
- Cardiac symptoms are seen with increased anemia and volume overload and should be treated accordingly.
- Treat concomitant hypertension, valvular disease, mitral valve prolapse and *cor pulmonale*.

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## OCULAR FINDINGS

Red blood cell sickling can occur in the microvasculature of the eye. Ocular findings, potentially blinding, can occur in the eyes of patients with sickle cell hemoglobinopathy including SS disease, SC disease and S $\beta$  thalassemia. Patients with sickle cell disease may show signs of the disease in their conjunctiva, uvea, retina and optic nerve. One of the most severe ocular complications is the development of proliferative sickle cell retinopathy, which may cause vitreous hemorrhage and retinal detachment with loss of vision.

Conjunctiva: scleral icterus and abnormalities of the conjunctival vessels are common. They may be observed with the slit lamp or a direct ophthalmoscope as widespread sludging of the blood and saccular dilatations in the conjunctival vessels (conjunctival sign). They are more common in SS disease and S $\beta^0$  thalassemia, than in SC disease and S $\beta^+$  thalassemia.

Uvea: segmental iris atrophy

Fundus: patients with SC disease frequently show the most severe fundus changes. The changes may be divided into nonproliferative and proliferative changes.

- Non-proliferative changes include retinal hemorrhages, schisis cavities, iridescent spots, black sunbursts, vascular occlusions, angloid streaks, and macular remodeling. These changes will rarely affect visual acuity.
- Proliferative sickle cell retinopathy can lead to blindness due to vitreous hemorrhage and retinal detachment. The mechanisms of sickle cell retinopathy are poorly understood. Sea fans are neovascular proliferation seen at the periphery of the perfused retina.
- Optic disk changes
- Neovascularization of the optic nerve and small optic nerve head have no visual significance.

HypHEMA (blood in the anterior chamber): When patients with sickle cell disease have hypHEMAs following trauma or eye surgery, they are at risk for developing elevated intra-ocular pressure. This can provide even moderate permanent deterioration of visual function. They need an immediate referral to an ophthalmologist for proper intervention.

Patients with sickle cell disease must undergo regular ophthalmologic evaluations starting at age 10 to detect ocular abnormalities. Indirect ophthalmoscopy and fluorescein angiography are required for proper evaluation of sickle cell retinopathy. Small lesions can be treated and progression to large lesions may be avoided. Safe and effective therapy is available for most of the ocular complications of sickle cell disease. Treatment, most frequently laser therapy, is available to obliterate aberrant vessels so as to prevent retinal hemorrhage and to treat detached retina.

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## PREGNANCY

Pregnancy in sickle cell disease has been the subject of much controversy. Some reports have described poor outcomes for both mother and child, and have advocated termination of pregnancy and sterilization of the woman, while others have reported successful outcomes. In a recent study of 286 pregnancies carried to delivery in women with sickle cell disease, it was reported that non-sickle-related antepartum and postpartum complication rates were comparable to those of African-American women who did not have sickle cell disease. The rates of morbidity due to sickle cell disease were the same during the pregnant and the non-pregnant state. There were no maternal deaths during the study. Ninety-nine percent of these pregnancies resulted in a live birth. This study, which represents the largest cohort followed to date, indicates that those caring for women with sickle cell disease should support them if they desire to have children.

The manifestations of pregnancy do not differ from those in women who do not have sickle cell disease. Thus, as many sources including textbooks and guidelines from the American College of Obstetricians and Gynecologists discuss these in detail, they will not be described here.

It is important to advise the mother that a possibility exists that her baby is at risk for sickle cell disease. The father should be tested. A CBC and hemoglobin electrophoresis are necessary for initial screening. Issues concerning genetic counseling can be found in other sections of these guidelines.

Since any of the complications of sickle cell disease may occur during pregnancy, the mother should be followed in a setting where more than routine obstetrical care is available. This is usually best achieved by continued follow-up by a sickle cell knowledgeable provider as well as attendance at a “high risk” obstetrical clinic. The management of sickle cell disease-related complications can be found in other sections of these guidelines. All surgical procedures, including termination of pregnancy and cesarean section should be performed under hematological guidelines. (See Surgery and Anesthesia.)

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## PRIAPISM

Priapism is a persistent painful erection of the penis and is quite common in association with sickle cell disease. It can occur at any age and may persist for hours, days, or even weeks. However, optimal therapy has not been defined.

The diagnosis of priapism is usually clinical and includes acute priapism, recurrent “stuttering” priapism, and chronic priapism. Episodes often begin during sleep and may be associated with dehydration, hypo-ventilation, and/or a full bladder. Both corporal bodies are turgid and tender and usually the glans penis and spongiosum are spared.

Minor episodes of priapism last less than three hours and may be recurrent. Major episodes last several days and are associated with a high risk of erectile dysfunction.

The physiology of priapism in sickle cell disease remains to be elucidated. Hemodynamic classifications include low flow “ischemic” priapism, which accounts for most episodes in adults, and high flow priapism, which may be more common in children. Blood flow in priapismic patients can be assessed by radionuclide penile scan or Doppler ultrasonography and flow assessment may be useful in directing therapy.

Management of priapism must include advice to seek medical attention if episodes exceed three hours in length or are recurrent. Priapism should be managed by a urologist and hematologist familiar with sickle cell disease. Management of a prolonged episode includes hospitalization, hydration, analgesia and often transfusion. Cavernal irrigation with an adrenergic agent is often utilized early in management. A glans-cavernosal (Winter procedure) or other shunt may be required in refractory patients. Early (< 48 hours) intervention, medical and/or surgical, may reduce the risk for subsequent impotence.

“Stuttering” episodes of priapism may be more amenable to conservative therapy and the prognosis is unclear. Patients with recurrent stuttering episodes ultimately may have a prolonged major episode, whereas pediatric and some adult patients may have resolution with normal sexual function. Stuttering episodes have been managed with cavernosal irrigation, sometimes administered by the patient at home. Other interventions include chronic transfusion, stilbestrol, hydralazine or pseudoephedrine administration. Again, the best management for priapism is not known and should be tailored to the individual patient by experienced practitioners. Prolonged episodes of priapism, with or without surgical intervention, may result in impotence. Patients with chronic priapism and sexual dysfunction can benefit from penile prostheses.

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## AVASCULAR NECROSIS (AVN)

Avascular necrosis (AVN) of the humeral and femoral heads affects patients with all types of sickle cell disease. The progressive destructive process is accompanied by varying degrees of pain and disability. AVN of the humeral head is usually less disabling than femoral AVN as the shoulder is a non-weight bearing joint. AVN can also be seen in other bones such as the knees and the spine.

The diagnosis of AVN is contemplated when the patient seeks medical treatment for acute pain in the hips, buttocks or shoulders with motion limitation because of the pain. The pain can be intermittent or become persistent. In early stages, x-rays of the shoulders or hips may appear normal, however, an MRI may demonstrate the early tissue damage associated with AVN.

An orthopedic specialist should be consulted for recommendations regarding treatment of AVN. Initial treatment includes analgesic (NSAID or narcotic), local heat, and restriction of weight-bearing. In children and teenagers, healing has been reported. For older patients with persistent pain in the hip and lesions seen on MRI examinations with minimal destruction of the joint, core decompression of the femoral head is an option. Other interventions such as hip fusion or reconstruction have also been utilized in adolescents and young adults with clinically significant and persistent disease.

For older patients with disabling hip necrosis or even patients in their early twenties with severe incapacitating hip pain, total hip replacement is the treatment of choice. AVN of the shoulders rarely requires surgical intervention.

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## LIVER/HYPERBILIRUBINEMIA

In sickle cell disease, there is chronic hemolysis and consequently icteric sclera due to increased level of mostly unconjugated bilirubin with a total bilirubin usually not exceeding 4mg/dl in a patient with normal liver function. The chronic hemolytic process also leads to production of gallstones (cholelithiasis), which can occur as early as two years of age. The prevalence of gallstones is 40% by age twenty. The increase in unconjugated bilirubin and consequently pigmented gallstones are typically most marked in SS disease and SB<sup>o</sup> thalassemia and much less in SC disease and SB<sup>+</sup> thalassemia.

The patient can be totally asymptomatic for many years, then develop symptoms. Patients may present with acute right upper quadrant or diffuse abdominal pain, nausea/vomiting, icteric sclerae, fever, and leucocytosis. The differential diagnosis should include acute cholecystitis, common duct obstruction with cholelithiasis, acute pancreatitis and acute hepatitis. In hepatic crisis, a clinical picture, simulating cholecystitis with right upper quadrant pain, nausea and vomiting, fever, and leucocytosis may occur in the absence of biliary tract disorder; conjugated bilirubin (direct) is also increased as in the case of cholecystitis or cholelithiasis with biliary obstruction. The work-up should include CBC, liver function studies, amylase/lipase, blood culture if significant temperature ( $\geq 101^{\circ}\text{F}$ ), abdominal sonogram/CAT scan/HIDA scan/ERCP as indicated. The patient with asymptomatic gallstones should not undergo surgery.

Management, as indicated by symptomatology, will include the following: intravenous fluid/NPO, analgesia, intravenous antibiotics, and transfusion or exchange transfusion. Conservative management is indicated in patients with acute cholecystitis and patients with hepatic obstruction unless there is evidence of common bile duct obstruction. ERCP may occasionally be therapeutic. Elective cholecystectomy should usually be performed within six weeks after the acute attack subsides. Laparoscopic cholecystectomy in experienced hands is preferred.

In childhood and adolescence, hepatic weight almost always exceeds standards for the normal population. Hepatomegaly appears to be due in part to the distention of the sinusoids by sickle cells. Acute and transient hepatomegaly may occur during a painful crisis and may be secondary to sinusoidal dilatation by circulating sickle cells. It is important to remember that hepatomegaly is present in 40% to 80% of patients with SS disease. It does not correlate with liver function tests that can be normal or slightly abnormal. With increasing age, liver function test abnormalities are common. This diagnosis can only be made through exclusion of the conditions discussed above.

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## KIDNEY/URINARY TRACT

Renal intravascular sickling is a very common event, which begins early in life and continues for the life of the patient. The hypertonicity and peculiar circulation in the renal medulla create an acidic and hyperosmolar environment where sickle red cells deoxygenate. The combination of hypoxia, hypertonicity and acidosis in the renal medulla leads to stasis in the vasa recta with consequent ischemia of the renal medulla and papillary tip. Hyposthenuria, nocturia and enuresis with decreased medullary blood flow (GFR) start early in life.

Renal papillary necrosis can be asymptomatic or accompanied by hematuria or proteinuria. As the patient gets older, renal tubular acidosis, potassium excretion deficit and proteinuria may be seen. In patients with SS disease, nephrotic syndrome associated with membranoproliferative glomerulonephritis has also been described. Chronic renal failure occurs in a small percentage of patients with sickle cell disease and is associated with end stage renal failure secondary to one or combinations of the renal events described above.

Renal disease is frequently asymptomatic, and therefore regular urinalyses should be part of the health maintenance visit. If there is persistent proteinuria and/or microscopic hematuria, a nephrology consultation should be obtained. Urine cultures should be performed for minimal indications. Reports indicate that chronic pyelonephritis may be more common in female adults with sickle cell disease, and that urinary tract infections occur more commonly in pregnant women with sickle cell disease than in pregnant black women without sickle cell. Urinary tract infections should be treated with vigorous antibiotic therapy. The patient with acute pyelonephritis should have careful, long-term monitoring with urinalyses, urine cultures and renal function studies at regular intervals. A renal sonogram with voiding cystourethrogram to exclude a predisposing anatomic or functional defect should be done in all previously unstudied patients and in those who present with a first episode of pyelonephritis.

Complications of untreated UTI include pyelonephritis and renal failure. Follow up of these patients should include frequent monitoring in consultation with the nephrologist and hematologist.

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## LEG ULCERS

Leg ulcers occur in 10-20 percent of patients with SS disease between the ages of 10 and 50 years of age and are more frequent in males. They can be very painful and are often accompanied by cellulitis and inguinal adenitis. Ulcers usually begin as small, elevated, crusting sores on the lower third of the leg above the ankle and over and around the medial and lateral malleolus, and occasionally over the tibial area or dorsum of the foot. After other causes of leg ulcers have been excluded, leg films and quantitative cultures from the base of the ulcer should be done.

Leg ulcers are difficult to treat and recurrence is common. Before treating the leg should be washed with mild soap and the slough should be removed from the ulcer base gently with gauze or cotton swab. Wet-to-dry dressings help to debride necrotic tissue and are applied every 3-4 hours with or without topical or systemic antimicrobial agents. They should be accompanied by bed rest for 7-10 days and leg elevation. Once granulation tissue appears, saline dressings can be used until the ulcer heals. If healing fails and the ulcer is not acutely infected, Unna's boot application is recommended for 2-3 weeks. The "boot" is left for one week.

Hyperbaric oxygen therapy and growth factors in gel form can enhance healing. Apply daily with the saline dressing or with an Unna's boot until healing begins. Skin grafts with artificial or patient's skin and free flaps may be tried for non-healing chronic ulcers. Before the graft or the flap is applied it is necessary to reduce the colony count of bacteria in the ulcer base by both debridement and the use of local antibiotics.

Blood transfusions can be used when the ulcer does not heal or if it progresses. Transfusions are given to raise the hemoglobin level to 10 g/dl and to decrease the hemoglobin S to less than 30%. After healing occurs, transfusions should be gradually discontinued. If there is no healing in 6 months, transfusions should be discontinued.

When ulcers heal, the scarred tissue is easily injured. Patients should be encouraged to wash their legs daily, to wear proper shoes and support stockings, and to report new ulcers promptly. Ulcers less than 2-3 cm have a greater chance of healing. If ulcers persist for more than 6 months they are considered chronic. Consultation with a plastic or vascular surgeon or referral to an ulcer center is recommended.

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## APPENDIX A

### PATIENT'S BILL OF RIGHTS

As a sickle cell patient/family member in New York State, you have the right to:

#### Receive quality care

- A trained medical interpreter if requested
- Seek and receive appropriate treatment without discrimination as to race, color, religion, sex, national origin, disability, sexual orientation, or source of payment.
- Request a provider that is sensitive and cautious in labeling any behavior as addictive. Providers must be made aware that some patients need frequent medical attention due to the variable nature of this chronic condition.
- Receive sensitive, culturally appropriate quality care in privacy.
- Know the names, positions and functions of any provider responsible for your or your family member's care.

#### Actively participate in care

- Request that the ED/urgent care setting consult with your provider/hematologist or with an affiliated hematologist in a timely manner. (Whenever possible contact your provider/hematologist before arriving at the emergency room.)
- Receive complete information about your diagnosis, treatment, and prognosis in the language in which the patient/family is proficient. You and your family must be allowed to ask questions to make informed decisions. Cultural beliefs need to be respected.
- Receive all the information you need to give informed consent for an order not to resuscitate. You also have the right to designate an individual to give this consent for you if you are too ill to do so. If you would like additional information, ask for a copy of the pamphlet, *Do Not Resuscitate Orders – A Guide for Patients and Families*.
- After being appropriately informed in your preferred language, the patient/family have the right to refuse treatment and be told what effect this may have on your health.
- Participate in research or refuse participation after receiving complete information and with the knowledge that your decision will not effect your medical care. The information must be culturally sensitive and ensure family involvement in decision making.

#### Parent/Provider Relationships

- Privacy and confidentiality of all information and records regarding your care.
- Participate in all decisions about your health care plan with an appropriate provider/hematologist. When you are discharged you must be provided with a written discharge plan and counseled in your preferred language.
- Review your medical record without charge. Obtain a copy of your medical record for which the hospital can charge a reasonable fee. You cannot be denied a copy solely because you cannot afford to pay.
- Receive an itemized bill and explanation of all charges.
- Complain without fear of reprisals about the care and services you are receiving and to have the hospital respond to you. If you request it, a written response must be provided. If you are not satisfied with the hospital's response you can complain to the New York State DOH. The hospital must provide you with the DOH telephone number.

## **APPENDIX B**

### **PATIENT'S RESPONSIBILITIES**

As a sickle cell patient/family member in New York State, you have the responsibility to:

- Provide, to the best of your knowledge, accurate and complete information about present complaints, past illnesses, hospitalizations, medications and other matters relating to your health and answer any questions concerning these matters in private.
- Follow the agreed health care plan and cooperate with the provider and other health care professionals responsible for your care.
- Report any unexpected changes in your conditions to the responsible provider. It is strongly advised that the patient/family bring with them an emergency room card.
- Participate in the development of your health care plan and discuss your concerns without reservations. You are responsible for periodically reassessing the health care plan in conjunction with the provider and for cooperating in making appropriate changes.
- Keep appointments, and when you are unable to do so for any reason, notify your provider.
- Fully discuss with the responsible provider your non-acceptance of proposed treatment and request alternative options (i.e., referral to comprehensive sickle cell program or appropriate provider) in order to receive optimal care.
- Respect and cooperate with health providers when seeking care.

## GLOSSARY

ACS – acute chest syndrome

AF – anterior fontanel

ARDS – adult respiratory distress syndrome

ASSC – acute splenic sequestration crisis

AVN – avascular necrosis

BC – blood culture

BUN – blood urea nitrogen

C (Hemoglobin C) – a variant hemoglobin present in 2-3% of African-Americans in the heterozygous, asymptomatic form

C/S – culture and sensitivity

CAT scan – computerized axial tomography

CBC – complete blood count

CNS – central nervous system

CO<sub>2</sub> – carbon dioxide

CVA – cerebrovascular accident

Dactylitis – the painful swelling of the hands and feet. The most common initial vaso-occlusive manifestation of sickle cell disease

DIC – disseminated intravascular coagulation

DIFF – white blood cell differential count

DOH – Department of Health

ECHO - echocardiogram

ED – emergency department

ERCP – endoscopic retrograde cholangio pancreatogram

ESR – erythrocyte sedimentation rate

Fetal hemoglobin quantitation – more precise quantitation of fetal hemoglobin. Routine hemoglobin electrophoresis is not accurate enough to establish the percentage of fetal hemoglobin or hemoglobin A<sub>2</sub>.

G6PD – glucose-6-phosphate dehydrogenase deficiency

GI - gastrointestinal

Genotypes –

SS = homozygous sickle cell anemia

SC = hemoglobin SC disease

Sβ = sickle beta thalassemia

Sβ<sup>+</sup> = sickle beta plus thalassemia

Sβ<sup>0</sup> = sickle beta zero thalassemia

GFR – glomerular filtration rate

GU – genitourinary

H/H – hemoglobin and hematocrit

Hb – hemoglobin. Protein in blood which makes it red and carries oxygen

Hct – hematocrit

HIV – human immunodeficiency virus

HPLC – high-performance liquid chromatography – a highly accurate technique for the identification of abnormal hemoglobins

IEF – isoelectric focusing – a more accurate technique to identify the hemoglobin bands compared to standard hemoglobin electrophoretic techniques

IVP – intravenous pyelogram

LCP – Legg-Calve-Perthes disease

LFT – liver function tests

MRA – magnetic resonance arteriography

MRI – magnetic resonance imaging

NPO – nil per orum (nothing by mouth)

NSAID – nonsteroidal anti-inflammatory drug (e.g. ibuprofen)

OSA – obstructive sleep apnea

Osteo – osteomyelitis

PCP – primary care provider

PRBCs – packed red blood cells

PT – prothrombin time

PTT – partial thromboplastin time

Retic - Reticulocytes

Rx - treatment

SCFE – slipped capital femoral epiphysis

Sickle cell preps – these are screening studies, e.g. Sickledex® and slide preparations with sodium metabisulfate, which simply identify the presence of sickle hemoglobin. They will NOT differentiate sickle cell trait from sickle cell disease, and will miss the lower concentrations of sickle hemoglobin present in the newborn.

SONO - Sonogram

SS Disease – Homozygous sickle cell anemia

TCD – transcranial Doppler

TRF – transfuse/transfusion

UA – urine analysis

UC – urine culture

URI – upper respiratory infection

US – ultrasound

UTI – urinary tract infection

VCU – voiding cystourethrogram

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