SICKLE CELL DISEASE AND TRAIT

CLINICAL AND COUNSELING PROTOCOL (CHILDREN 0-6 YEARS) HAWAI`I

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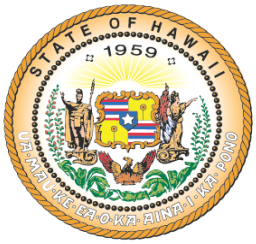

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Questions or Comments?

For more information, please contact the Hawai`i State Genetics Program at 808-733-9055 or you can visit our website at www.hawaiigenetics.org

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Introduction

As an activity of the Hawai`i Sickle Cell Project (funded by a Health Resources and Services Administration grant), this protocol was developed for distribution to Emergency Departments, primary care physicians, nurses, allied health workers, and health clinics in Hawai`i. This protocol sets forth a program for identifying, diagnosing, and treating newborns and infants with sickle cell disease or sickle cell trait. It also recommends education and counseling strategies for parents and caregivers. It is intended that this protocol will provide basic information to those caring for individuals with Sickle Cell disease or Sickle Cell trait in Hawai`i. The references listed at the end of the protocol include detailed medical management and health supervision information, for those wishing to research further.

What is Sickle Cell Disease?

Sickle Cell disease (SCD) is an inherited blood disorder that results in abnormal hemoglobin. Hemoglobin is a component of red blood cells that usually carries oxygen throughout the body. People with Sickle Cell disease have red blood cells that sickle, or change shape. The sickled cells have difficulty moving through blood vessels, which can result in a lack of oxygen to tissues and pain for the individual.

Sickle Cell disease is an autosomal recessive condition. Two parents who are carriers of a hemoglobin gene mutation (also referred to as a "trait") have a 25% chance of having a child with Sickle Cell disease. There are several gene mutations which can combine to result in a form of Sickle Cell disease. The most common combination is "SS" (two copies of "S" trait), but other combinations can include "SC" and "S/ß-thalassemia".

Carriers do not generally have signs and symptoms. People with Sickle Cell disease, however, can experience infections, pain, anemia, organ damage, and other symptoms. It is important that people with Sickle Cell disease are cared for closely by a primary care physician. Hematologists, geneticists, pain management specialists, nurses, genetic counselors, and social workers may also be involved in caring for a person with Sickle Cell disease.

HAWAI`I: NEWBORN SCREENING IDENTIFICATION AND FOLLOW-UP

Protocol Overview

Hawai`i infants' newborn screening samples are collected and sent to Oregon State Public Health Laboratory (OSPHL).

The OSPHL informs the infant's **primary care physician (PCP)** of the newborn screening results.

The OSPHL returns the results to the Hawai`i **Newborn Metabolic Screening Program (NBMSP**).

The NBMSP provides the PCP with educational materials and referral information for the Hawai`i Community Genetics (HCG) Hemoglobinopathy Clinic

As the Medical Home, the PCP manages the patient's care, and makes appropriate referrals.

Long-term tracking of individuals with SCD

PCP Referral Options

hematologist

Hawai`i Children with Special Needs Program (808-733-9055) for eligible families

Hawai`i Community Genetics (HCG) Hemoglobinopathy Clinic

Patient/family is seen by a hematologist and the genetics team for evaluation and genetic counseling

Recommendations for testing, medical management, etc. are made to the PCP

Recommended Community Follow-Up

Appointment #1: Hematology

- ❑ Genetic Counselor:
  - ✓ takes measurements
  - ✓ creates pedigree
  - ✓ completes clinic intake
  - ✓ psychosocial support
  - ✓ provides family with educational resources
  - ✓ completes and sends laboratory testing paperwork
- ❑ Hematologist:
  - ✓ completes hematology counseling
  - ✓ generates letter for referring physician and family

Appointment #2: Genetics team

- ❑ scheduled once outstanding laboratory results are received
- ❑ Genetic Counselor:
  - ✓ provides genetic counseling
  - ✓ provides patient literature
  - ✓ generates individualized fact sheet for physician and family, based on laboratory results
- ❑ Geneticist:
  - ✓ provides genetic counseling
  - ✓ generates one letter for physician and family

** Depending on the result of the newborn screen, the clinic appointment(s) may be altered (i.e., if a newborn is identified as having sickle cell trait, only one visit with the genetics team may be necessary).

Comprehensive Sickle Cell Disease or Trait follow-up services are available from:

Hawai`i Community Genetics Hemoglobinopathy Clinic

1441 Kapiolani Blvd. #1800
Honolulu, HI, 96814
Tel: (808)973-7303
Fax: (808)973-3401

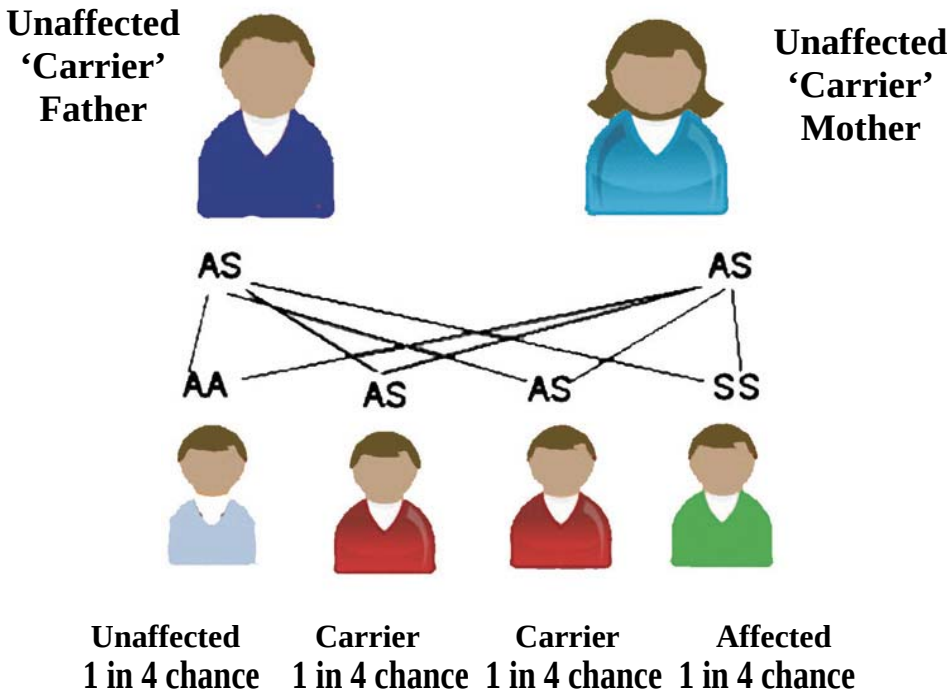
GENETIC COUNSELING FOR SICKLE CELL DISEASE (SCD) AND SICKLE CELL TRAIT (SCT)

The goals of sickle cell disease and trait counseling following a positive newborn screen and/or confirmatory testing are to:

i provide an understanding of the inheritance of SCD and SCT

ii provide options for medical management

iii provide information and support needed to make family planning decisions



Basic Content for all Sickle Cell Disease Sessions

- ❑ Purpose and goal of the session
  - ✓ review newborn screening results and discuss implications
  - ✓ address concerns and questions of the family
- ❑ Definition of condition
  - ✓ What is SCD?
  - ✓ What is SCT?
  - ✓ What is the difference between the SCD and SCT?
  - ✓ Which traits have combined in the child to cause SCD?

- ❑ Health problems that can occur in SCD
  - ✓ variability of and inability to predict occurrence and frequency of health problems in SCD
  - ✓ average life span of individuals with SCD
- ❑ How sickle cell conditions are acquired— genetic basis
  - ✓ potential outcome of each pregnancy if both partners have SCT or another contributing trait
    - potential of "S" trait to combine with other traits ("C", ß-thalassemia)
    - testing and the potential to identify non-paternity
  - ✓ potential future pregnancy outcomes for patient with SCD
  - ✓ autosomal recessive inheritance
  - ✓ ethnic groups who have higher rates of SCD and the percent of individuals in the counselee's racial group who have SCT and SCD
- ❑ Medical management recommendations
  - ✓ option to attend Hemoglobinopathy Clinic on a regular basis (yearly) for education and family counseling
  - ✓ regular appointments with hematologist
  - ✓ "In Case of Emergency" – emergency signs and symptoms that should prompt parents to call the doctor/ER immediately:

FEVER	101°F or higher
HEAD	severe headache or dizziness
CHEST	pain or trouble breathing
STOMACH	severe pain and swelling
COLOR	very pale
PENIS	painful erection
BEHAVIOR	seizures; weakness or paralysis (can't move arm or leg); can't wake up

- ❑ Family planning options

Basic Content for all Sickle Cell Trait Sessions

- ❑ Purpose and goal of the session
  - ✓ review newborn screening results and discuss implications
  - ✓ address concerns and questions of the family
- ❑ Definition of condition
  - ✓ What is SCT?
  - ✓ What is the difference between SCT and SCD?
  - ✓ What other traits may also combine with SCT?
- ❑ Health problems that can occur in SCD
  - ✓ variability of and inability to predict occurrence and frequency of health problems in SCD
  - ✓ average life span of individuals with SCT and SCD
- ❑ How sickle cell conditions are acquired— genetic basis
  - ✓ potential outcome of each pregnancy if both partners have SCT or another contributing trait
    - potential of "S" trait to combine with other traits ("C", ß-thalassemia)
    - testing and the potential to identify non-paternity
  - ✓ autosomal recessive inheritance
  - ✓ ethnic groups who have higher rates of SCD and the percent of individuals in the counselee's racial group who have SCT and SCD
- ❑ Medical management recommendations
  - ✓ option to attend Hemoglobinopathy Clinic on an as-needed basis for education and family counseling
- ❑ Family planning options

Intended Learning Outcomes for Counselee

- ❑ The difference between sickle cell trait and sickle cell disease.
- ❑ SCT is not an illness, so no restrictions need to be placed on activities; other traits are not illnesses, either.
- ❑ Both parents must have SCT or another abnormal hemoglobin trait for their child to have SCD.
- ❑ There is a 25 percent chance that each pregnancy will result in a child with SCD if both parents have SCT.
- ❑ Natural history of SCD (including potential health problems, variability of severity, resources necessary to care for a child with SCD, life span, etc.).
- ❑ Options for medical management.
  - SCD – regular, yearly appointments
  - SCT – as-needed basis
  - "In Case of Emergency" awareness
- ❑ The family planning options available to persons with SCD and SCT.
- ❑ Reasons couples might decide to have or not have children if both have SCT.

Instructional and Educational Techniques

- ❑ Use lay language and common words for scientific terms whenever possible.
- ❑ Use visual aides to illustrate key points.
- ❑ Establish a dialogue/discussion rather than a lecture or information-giving format.
- ❑ Implement a pre- and post-assessment of the session.
- ❑ Use the post-assessment as an opportunity to clarify misinterpretation or uncertainties about the information discussed during the session.
- ❑ Provide literature written in lay language covering the essential facts.
- ❑ Make available sources of more detailed information for those who are interested.
- ❑ Communicate the availability of the provider for any follow-up questions.
- ❑ Provide a full description of the material covered, including a copy of all graphics, plus a summary of the highlights or key points in the form of a fact sheet.
- ❑ Genetic counseling for decision-making assistance will be nondirective and objective. Counselors will not introduce personal biases or offer specific recommendations.
- ❑ Follow a standard protocol to ensure that the essential topics are covered.

MEDICAL MANAGEMENT ISSUES

** It is important to stress health care maintenance, compliance with prescribed prophylactic penicillin, and the prompt medical evaluation of the child at times of acute illness.**

Frequent Doctor/Clinic Visits

Children with SCD or SCT should receive the same general health care as children without SCD or SCT. Well-child visits for growth monitoring, immunizations, and counseling on preventive health measures should be supplemented with specific information about SCD.

The schedule of well-child visits is:

AGE	HOW OFTEN
0-6 months	every month
6-12 months	every two months
1 year to 5 years	every 3-4 months

This schedule may be modified depending on the need of the patient with SCD, and may include visits with a hematologist after referral by the primary care physician. Genetic counseling is recommended for all newly ascertained cases and, thereafter, on a follow-up basis.

Common Laboratory Tests

A child with SCD will likely have to provide blood and urine samples. Some of the common tests that might be ordered include:

Hemoglobin Electrophoresis

- ❑ determines a person's hemoglobin type and the type of SCD they have
- ❑ done before blood transfusions to decide how much blood should be given, and after transfusions to determine if enough blood was given to prevent the complications of sickling

Complete Blood Count (CBC)

- done to find out the number, shape, and size of the red blood cells, and the hemoglobin level

Hemoglobin Level	
child without SCD	11-14
child with SCD	6-10

- if the child's hemoglobin level is less than 6, s/he may need to be taken to the hospital and transfused

Reticulocyte (Retic) Count

- determines the level of the young red blood cells
- to determine if the bone marrow is properly making and releasing new red blood cells

Kidney and Liver Function tests

- to determine if the organs have been damaged by SCD

Urine tests (urinalysis)

- urine is checked under a microscope for signs of infection

Blood Chemistry tests

- measure substances that are important for health and growth

X-Rays

- to determine if there is an infection in the lungs
- to determine if bones have been damaged by SCD

Immunizations

Like other children, children with SCD will receive the usual immunizations against hepatitis B, polio, diphtheria, pertussis, tetanus, Haemophilus influenza type b, measles, mumps, and rubella. Children with SCD will also require additional immunizations to help fight infections.

The pneumococcal conjugated vaccine (PCV) is important for those with SCD. The American Academy of Pediatrics (AAP) recommends Prevnar for children with SCD up to 59 months old.

Meningococcal vaccination has not been recommended routinely for children at most U.S. sickle cell centers, probably due to infrequent meningococcal infections reported. If children live in or travel to areas with a high prevalence of meningococcal infection, this vaccine should be given.

Influenza vaccination is recommended seasonally for patients with SCD.

Pneumonia

Pneumonia is very common in people with sickle cell disease. A blood culture for infection and a chest x-ray should be ordered to make this diagnosis. Treatment includes intravenous antibiotics. If sickling of the red blood cells occurs in the lungs (lung infarction), administration of an oxygen mask or a blood transfusion may be necessary.

Penicillin Prophylaxis

The *most important intervention* in the routine management of children with SCD is penicillin prophylaxis. Infection is the leading cause of death in children with SCD, so parents should be encouraged to continue this essential intervention. ***Penicillin should be started no later than two months of age.***

Penicillin is given by the following schedule:

Age	Frequency
2 months to 3 years old	125 mg twice per day
over 3 years old	250 mg twice per day

If a child is allergic to penicillin, erythromycin can be given instead (erythromycin ethyl succinate (20 mg/kg) divided into two daily doses). Most doctors recommend that children receive penicillin until age 5 years. The benefits of receiving penicillin beyond 5 years of age are not proven though, given that children with SCD older than 5 years of age still lack splenic function, parents should be given the option to continue penicillin prophylaxis.

Penicillin may be given as a liquid or tablet. Finely crushed pills may be given to young children, mixed with food such as applesauce, ice cream or yogurt. Pills have an important advantage because they are stable for years, compared to liquid forms of penicillin that must be refrigerated and then discarded after 2 weeks. An alternative to oral penicillin is an injection of 1.2 million units of long-acting Bicillin™ every 3 weeks.

Parents must be taught to recognize early signs and symptoms of specific complications, including fever, splenic sequestration crisis, respiratory distress, and dehydration. Appropriate medical follow-up includes regular visits to assess the infant's medical status and the administration of age-appropriate immunizations.

Standard antibiotic prophylaxis should be used to cover dental procedures such as extractions and root canal therapy.

Transfusions

Children with SCD may need transfusions (simple or exchange) due to:

- ❑ severe anemia (splenic sequestration or aplastic episode)
- ❑ stroke or history of high risk of stroke
- ❑ pneumonia
- ❑ priapism
- ❑ surgery

Potential complications of transfusions, including infection, allo-immunization, designated donors and allergic reactions, should be discussed with the family of the child with SCD.

Children who require chronic transfusions can develop iron overload. ***Excess dietary iron should be avoided.*** Chelation therapy must be discussed with the family and initiated so as to prevent damage to the child's organs. While chelation therapy was previously administered as a daily, 8-12 hour subcutaneous infusion, the first oral chelation therapy was approved by the U.S. Food and Drug Administration in November 2005.

Nutrition

Nutrition counseling is an important part of routine health care. Mothers should be encouraged to breastfeed their infants; iron fortified formulas are an alternative. Additional iron should *not* be given *unless* the patient is confirmed to have iron deficiency, since people with SCD accumulate iron faster than normal. Microcytosis in children with SCD could be due to a thalassemia trait rather than iron deficiency.

Children with SCD need more fluids than other children, and will usually get thirsty more often. If the child has a fever, is in pain, is active, or it is very hot outside, s/he should intake a greater amount of fluids. Most children with SCD have bedwetting episodes, for which there are strategies such as waking the child during sleep to urinate.

Folic acid (1 mg orally) should be given daily to patients with chronic hemolysis, such as those with SCD, to reduce the risk of bone marrow aplasia. Folic acid may be provided once a child is one year old.

Deficiencies in nutrients (e.g., zinc) should be corrected if they occur. Fluoride, given in vitamins or in drinking water, will help to prevent dental caries.

Fever

Fever is one of the most common signs of illness in children, and most parents are unaware that their child could die from the infection that is causing the fever. Particularly with children who have SCD, it is important to recognize the signs of a fever.

***Signs of a fever*:**	rectal temperature > 100-101° oral temperature > 100° axillary temperature > 99°

Parents should be discouraged from giving antipyretics at home at the first sign of fever. A history of fever should be taken seriously, and healthcare workers, particularly those in emergency rooms, should not challenge parents whose children may have no or only low-grade fever on presentation. At a minimum, the well-looking, non-febrile child should be observed in the emergency room for a few hours to determine if fever or other signs of infection develop.

All children with SCD who have fever (>38.5ºC or 101ºF) and other signs of infection (chills, lethargy, irritability, poor feeding, vomiting) should be evaluated promptly. The younger the child, the higher should be the index of suspicion. In a child with no obvious source of infection, a minimum evaluation should include blood culture, complete blood count, reticulocyte count, and chest x rays (for those younger than 3 years of age). Immediately after the blood is taken, the child should be given broad-spectrum antibiotics, preferably intravenously. Broad-spectrum antibiotics should be given even if these tests cannot be performed. In areas of the world where malaria is endemic, antimalarial treatment should be added to the antibiotic coverage. Further management protocols vary by locality.

Bacterial infection is the major reason for concern about the febrile child with SCD, but other complications should not be overlooked: acute splenic sequestration and erythroid aplasia ("aplastic crisis") are commonly associated with fever. An aplastic crisis causes production of red blood cells to halt for 10 days. Since the red blood cells in children with SCD survive only 10-15 days (compared to 120 days in children without SCD), the blood count (hemoglobin & hematocrit) drops rapidly to dangerously low levels during an infection.

Pain Episodes

Painful events are common in children with SCD, though not in very young children. The earliest complication observed clinically is often dactylitis ("hand-foot syndrome" or painful swelling of the hands and feet), which starts at less than 1 year of age.

Typical vaso-occlusive pain may involve limbs, abdominal viscera, ribs, sternum, vertebrae, and sometimes skull bones. Pain episodes can start suddenly, or they may follow an illness along with decreased activity, loss of appetite, and increased jaundice.

Parents should be assured that most pain episodes have no identifiable precipitating factors, so they should not blame themselves or their children. Likewise, health care providers should not assume that the pain is due to the fault of the parent.

Children with pain should be evaluated. Parents should be taught to localize the exact site of pain, to ensure that a limp is due to pain and not weakness, and to assess the degree of pain for appropriate treatment.

The object of pain management is relief. Often, extra fluids and reducing activity levels can ease pain. A warm bath, heating pad, or massage may also relieve pain.

Parents should be taught proper analgesic use in order to manage most pain episodes at home. Medications given for mild and moderate pain include acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, and mild opioids, such as codeine, for young children. Stronger NSAIDs and opioids are reserved for older children with severe pain. Parents should be educated about the side effects of these drugs and reassured about the risk of drug addiction when they are used properly. If home management fails, parents should be encouraged to call for consultation or a hospital visit.

Parents should be encouraged to contact their doctor/clinic if their child experiences any of the following symptoms:

- ✓ chest pain or shortness of breath
- ✓ abdominal pain
- ✓ pain associated with fever or swelling and redness
- ✓ pain that is not relieved by home remedies
- ✓ severe headache or dizziness
- ✓ for males, a painful erection

Problems with the Spleen

Most children with SCD will have enlarged spleens within the first two years of life. A baseline evaluation of spleen size done when the child is healthy is helpful for comparison. Children with SS will have an enlarged spleen for several years but by age six the spleen will reduce in size due to scarring. Children with scarred spleens may have more infections than typically expected.

Splenic sequestration can occur when the spleen enlarges rapidly and traps red blood cells. This can lead to heart failure and death if a blood transfusion is not performed immediately. If a child has a fever or cold, abdominal swelling or pain, is pale and tired, these could be signs of splenic sequestration. A splenectomy can be performed if a child is at least two years old. This will prevent future splenic sequestration episodes.

Problems with Kidneys and Urine

Children with SCD can become dehydrated more easily due to damage to the kidneys caused by sickled cells. Infections in the bladder and kidneys can also occur. Treatment includes antibiotics and subsequent urine analysis to detect the presence of infection. Blood may appear in the urine due to bleeding from the kidney. This should be assessed to determine the cause.

Gallstones

About one third of children with SCD will develop gallstones by the age of seven years. Physicians should evaluate children with SCD for signs of a gallstone that has become stuck in the gallbladder duct (yellow eyes, pain in the right side of the abdomen). Parents should also be educated to be aware of these signs.

Stroke

Less commonly, children with SCD can be affected by strokes; < 1/20 children with SS disease (two Sickle hemoglobin genes) will have a stroke. Parents should be educated as to the signs of a stroke (fainting, sudden weakness, asymmetrical movement of the face, severe headache, difficulty speaking, limping) and encouraged to bring their child to the doctor/clinic. To prevent a recurrence, children who have had one stroke are transfused monthly for 3-5 years following the first stroke.

Delayed Growth

Some children with SCD are shorter and thinner than other children their age. Puberty may also be delayed. The difference in size is usually temporary, as children with SCD will keep growing longer after their peers have stopped growing. They will generally reach the height that is expected, given their parents' sizes.

Priapism

Priapism can occur at any age. If a child has episode when the penis becomes hard and painful, then becomes soft again (also called "stuttering priapism"), they should be encouraged to discuss this with their doctor. Priapism lasting longer than a few hours requires blood transfusions and, in rare cases, surgery.

Activities

Children with SCD should avoid activities which expose them to extreme temperatures (swimming in cold water) or altitudes (backpacking, hiking, and skiing). If participating in these activities, children should plan for temperature differences (i.e., use of gloves, warm clothes) and approach activities with caution and prevention of symptoms in mind. Children with SCD can participate in other normal activities, but should make sure to stay hydrated and rest when tired.

In Case of Emergency

Parents should call their primary care provider for advice if any of the following occurs:

Stomach:	Vomits more than once; has diarrhea more than once
Color:	Jaundiced (eyes or skin look yellow)
Arms, Leg, Back:	Pain with no other symptoms
Chest:	Coughs without fever or chest pain
Nose:	Runny or stuffed nose
Behavior:	Isn't acting right; refuses to take penicillin; is less active than usual; refuses to eat or drink

Parents should call their primary care provider or go to the emergency room immediately if any of the following signs are present:

Fever:	101 F or higher
Head:	Severe headache or dizziness
Stomach:	Severe pain or swelling
Color:	Very pale
Penis:	Painful erection
Behavior:	Seizures; weakness or paralysis (can't move arm or leg); can't wake up

RECOMMENDATIONS FOR PRIMARY CARE PHYSICIANS

Specific physical, laboratory, and other evaluations are needed to monitor children with SCD.

Comprehensive Care Plan for Children with SCD

The comprehensive management of SCD often requires a team that includes doctors, nurses, health educators, and social workers. Often, emergency room physicians, radiologists, anesthesiologists, surgeons, and critical care specialists also become involved. Facilities generally should have medical consultants, hematology and microbiology laboratories, a radiology service, and a blood bank available 24 hours a day. On occasion, patients may need Transcranial Doppler (TCD) ultrasonography, computerized axial tomography, magnetic resonance imaging (MRI), neuropsych testing and MRI with angiography, which are available at major medical centers.

After the diagnosis of SCD, the comprehensive care team must initiate and coordinate medical and psychosocial care for the child and family. These activities should include education, genetic counseling, and preparation for independent living.

For children ages 0-6 years, the following Care Plan is recommended by Children's Hospital Oakland Sickle Cell Center:

EVALUATION	INTERVAL
General Physical Examination Under 6 months 6 months to one year 1-6 years	 once per month every 2 months every 3-4 months
Immunizations	ask your doctor about schedule
TB Tests	once per year, starting at 12 months
Social Worker Evaluation Interview Home Visit School Assessment	 every 2 years once per year once per year
Genetic Counseling Family Studies Counseling and Education	 first visit 1-3 times per year
Hematology (red blood cell) Evaluation	every 3 months to once per year
Liver Studies	once per year
Gallbladder Evaluation	every year or when needed
Renal (kidney tests)	once per year or when needed
Cardiac (heart tests)	every 2 years
Pulmonary (lung tests)	when needed; baseline eval at 5 years
Dental Evaluation	once per year, starting at age 3
Psychological/Family Therapy Consultation	once per year
Physical Therapy Assessment	when needed
Developmental Screen	once per year or when needed
Formal Nutrition Assessment	every 2 years or as needed

* Transcranial Doppler (TCD) ultrasonography should also be performed by the age of two years; repeat annually if normal and every four months if TCD is marginal.

Physical Examination

SCD in young children has a variable presentation. The earliest physical sign may be jaundice in the first few weeks of life. If hemolysis is not clinically significant, family members should be reassured about eye color changes so as to reduce anxiety.

Hepatomegaly is a common finding in children with SCD; the cause is unknown, but it does not signify liver dysunction. Spleen size should be measured, as most young children with SCD will get an enlarged spleen sometime in their first two years of life. A splenectomy may be performed; if a child has one splenic sequestration, s/he is more likely to have another.

Organomegaly leads many children with SCD to have a protuberant abdomen, often with an umbilical hernia.

Almost all SCD patients with moderate-to-severe anemia have a cardiac systolic flow murmur that does not require further evaluation. Parents should be reassured about the murmur so that they will not be alarmed when other doctors and nurses notice it.

Bone marrow expansion often causes maxillary hypertrophy with overbite; orthodontics are recommended to prevent or correct this.

Growth and development should be followed closely in children with SCD, and nutrition should be optimized. Children and parents should be counseled about potential social problems related to short stature and delayed sexual development, which can greatly affect adolescents. Most children with SCD do not require a special diet or vitamins. Most youth with SCD will, in fact, continue growing once their peers have finished, thus reaching the height that would be expected from the size of their parents.

Infection is the leading cause of death among children with SCD. It is important to educate parents to recognize the signs of infection (fever, shortness of breath, rapid breathing, tiredness, chest pain) and to have them bring their child to the doctor/clinic for treatment. The child may have to be admitted to the hospital for administration of intravenous antibiotics.

Laboratory Evaluation

It is useful to collect a series of baseline values on each patient with SCD. These values can be compared with those reported at times of acute illness.

Typically, children should have the following routine clinical laboratory evaluations:

Age	Test	Frequency
3 – 24 months	CBC with WBC differential	every 3 months
> 24 months	CBC with WBC differential	every 6 months
6 – 24 months	percent Hb F	every 6 months
> 24 months	percent Hb F	annually
≥ 12 months	renal function (creatinine, BUN, urinalysis)	annually
≥ 12 months	hepatobiliary function (ALT, fractionated bilirubin)	annually
≥ 12 months	pulmonary function (transcutaneous O_2 saturation)	every 6 months

Special Studies

The brain and lungs are among the organs which are most susceptible to serious damage in individuals with SCD. Early detection of dysfunction may allow intervention to reduce risk of further damage.

Brain

Transcranial Doppler (TCD) ultrasonography , magnetic resonance imaging (MRI) with or without angiography, and neuropsychometric (NPM) studies have been used extensively to evaluate children with SCD.

TCD screening of children with SCD-SS is recommended to begin at 2 years of age and continue annually if TCD is normal and every 4 months if TCD is marginal. An abnormally high blood flow velocity by TCD in the middle cerebral or internal carotid arteries is associated with an increased risk of stroke; however, blood flow results should be interpreted cautiously because they are dependent on the technique employed. Abnormal results should be repeated within 2 to 4 weeks. Prophylactic chronic blood transfusion is an option for patients with an increased TCD flow velocity.

Children with SCD who have "silent" cerebral infarcts detected by MRI have a higher rate of abnormal NPM studies and a higher risk for overt strokes. Stroke prevention strategies based on abnormal MRI results have not been tested, but children with abnormal MRI or NPM studies could be evaluated more frequently and carefully and considered for therapeutic measures.

Lungs

Children with SCD frequently have abnormal pulmonary function tests (PFT). PFT should be done regularly in those individuals who have a history of recurrent acute chest episodes or low oxygen saturation. Lung function declines with age, so it is important to identify those who need close monitoring and treatment.

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Sickle Cell Disease Guideline Panel. *Sickle Cell Disease: Screening, Diagnosis, Management, and Counseling in Newborns and Infants.* Clinical Practice Guideline No. 6. AHCPR Pub. No. 93 0562. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, U.S. Department of Health and Human Services. April 1993.

RESOURCES

For more information about Sickle Cell Disease and Sickle Cell Trait, please visit the following websites:

American Academy of Pediatrics Health Supervision Guidelines
http://aappolicy.aappublications.org/cgi/content/full/pediatrics;109/3/526

Gene Reviews
http://www.geneclinics.org/query?dz=sickle

March of Dimes
http://www.marchofdimes.com/professionals/681_1221.asp

Medline Plus
http://www.nlm.nih.gov/medlineplus/sicklecellanemia.html

National Heart Lung and Blood Institute
http://www.nhlbi.nih.gov/health/dci/Diseases/Sca/SCA_WhatIs.html

National Human Genome Research Institute
http://www.genome.gov/10001219

National Office of Public Health Genomics:
http://www.cdc.gov/genomics/hugenet/reviews/sickle.htm

Sickle Cell Disease Association of America
http://www.sicklecelldisease.org

Sickle Cell Information Center
http://www.scinfo.org

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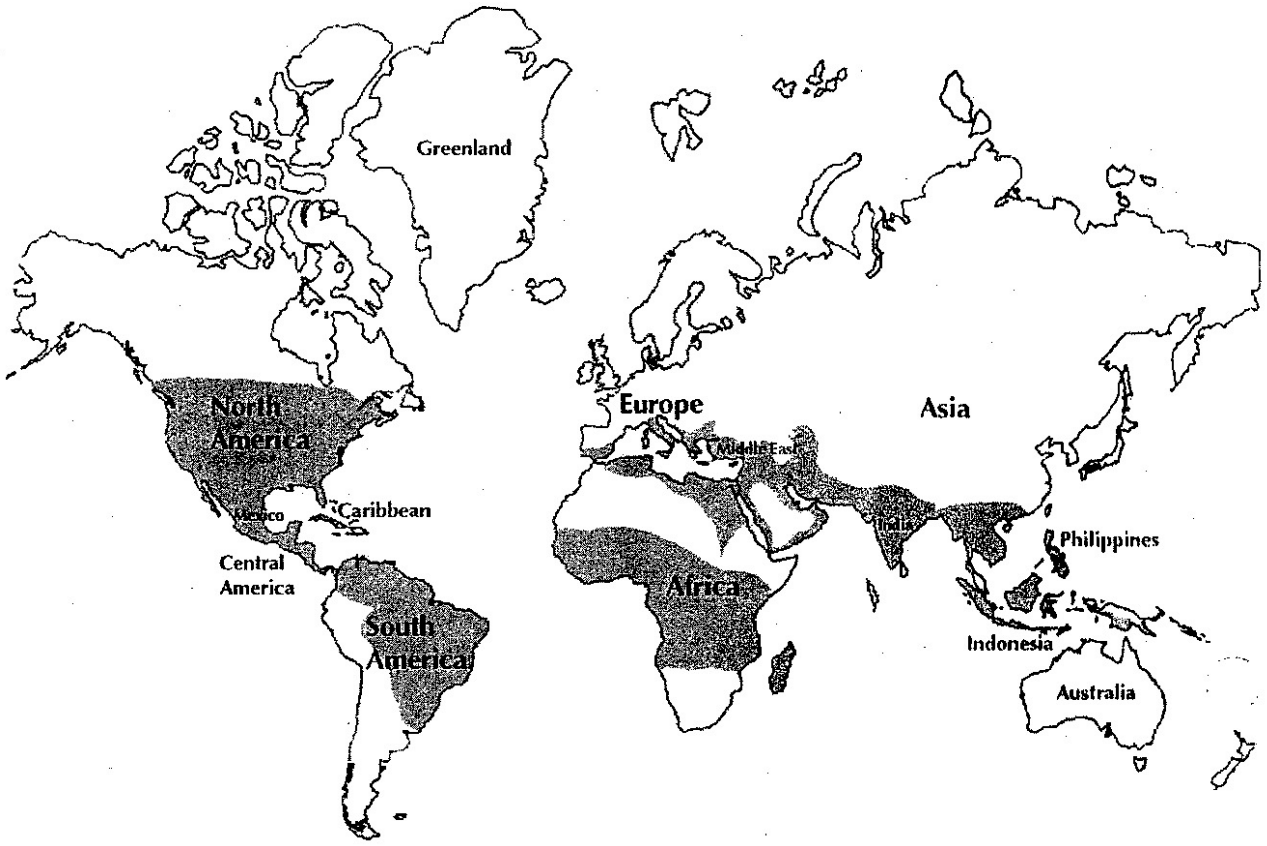
Mahalo Nui Loa!!

In addition to parts of Africa, South America, the Caribbean and South-East Asia, people whose ancestors are from the shaded parts of the world are more likely to have hemoglobin variants such as S, C, E, or B-Thalassemia.



Adapted from Genetic Disease Branch, Newborn Screening Program, 5/05