New England Pediatric Sickle Cell Consortium

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Routine Health Care Maintenance of Pediatric Patients with Sickle Cell Disease

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Disclaimer Statement:

- Hospital clinical pathways are designed to assist clinicians by providing an analytical framework for the diagnosis and treatment of specific medical problems. They may be used for patient education and to assist in planning future care. They are not intended to replace a physician's judgment or to establish a protocol for all patients with a particular condition. The ultimate decision regarding the care of any patient should be made in respect to the individual circumstances presented by the patient.
- Any specific medications and dosing must always be reviewed carefully for each patient in view of any history of drug allergy or adverse reactions.
- This document was based on available research and clinical experience at time of its compilation.
- The following protocol is a regional guideline, and may be adapted by individual institutions as needed.

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Routine Health Care Maintenance

This document is intended to identify routine health maintenance issues important in the care of children with sickle cell hemoglobinopathies and to aid primary care physicians and hematologists who together provide the medical home for these patients.
This is meant as a supplement to, not a substitute for, age-appropriate routine health maintenance for children and adolescents.

Inclusion: all children and adolescents with sickle hemoglobinopathies (including but not limited to HbSS, HbSC, HbS-β^0 thalassemia, HbS-β^+ thalassemia, $HbSO_{Arab}$, HbSD). These will be collectively referred to as sickle cell diseases (SCD).

I. Introduction

- Identification of infants with sickling disorders by newborn screening for hemoglobinopathies, followed by a program of comprehensive care, has significantly reduced mortality and morbidity in the United States.
- While sickling disorders are chronic and sometimes life-threatening, the majority of patients are expected to survive well into middle-age and beyond.
- Sickling disorders produce functional asplenia, which results in compromised immunological response and at increased risk of invasive encapsulated bacterial infections. There are particular susceptibilities to Streptococcus pneumonia (Pneumococcus), Haemophilus influenza b (Hib), and Neisseria meningitidis (Meningococcus).
- Highest infectious mortality rates are in children ages 1 to 3 years.
- Prophylactic penicillin from early infancy has reduced serious pneumococcal infections, but has not been shown to be helpful for older children.
- Leading causes of morbidity for older children and adolescents include recurrent severe vaso-occlusive episodes, acute chest syndrome and stroke.
- Recurrent acute chest syndrome and/or baseline reactive airway disease may predispose children to future pulmonary compromise.
- In adult patients pulmonary hypertension is linked to increased mortality.
- Transcranial Doppler (TCD) screening identifies children at increased stroke risk allowing introduction of effective, preventative therapy. Regular TCD screening has become the standard of care for children with HbSS and HbS-β^0 thalassemia disease. Screening is not routinely performed for HbSC, HbS-β^+ thalassemia and other compound heterozygote diseases.
- Ophthalmological consequences of SCD begin with asymptomatic proliferative retinopathy, and can progress to retinal detachment and vision loss, especially in patients with Hb SC disease.
- Hydroxyurea treatment in sickle cell anemia reduces morbidity in adult and pediatric patients and improves mortality in adults. While most data are from adult subjects, newer studies have shown safety and tolerability of hydroxyurea in pediatric patients. Side effects include reversible neutropenia and an unobserved potential carcinogenicity and teratogenicity.

II. Visit Frequency with Comprehensive Hematology Program:

First 24 months of life	q 3-4 months
> 2 years – 12 years	q 6 months
> 12 years	q 6-12 month

* *More frequent visits may be required for patients with increased educational needs, accumulated complications, and therapeutic monitoring (e.g. hydroxyurea and chronic transfusion therapy).*

III. Elements of Comprehensive Visits

Should include, but not be limited to:

- Medication Review: including prophylactic medication and home pain plan
- Interval History: Inquire about fever, painful episodes, respiratory symptoms, priapism, neurological symptoms, splenic sequestration, nocturnal enuresis, snoring, ED visits, admissions, transfusions and missed school
- Physical Examination:

Vital Signs: growth parameters, oxygen saturation (RA) and blood pressure
HEENT- tonsillar hypertrophy, scleral icterus, ophthalmoscopy
CV- cardiac murmur
Abd- hepatosplenomegaly, right upper quadrant discomfort
GU- priapism, penile fibrosis
Ext- shoulder and hip ROM, leg ulcers, extremity myotomes

- Educational Review[1]:

Should begin from infancy and be reinforced at each visit. Document topics covered and remaining educational needs. As child matures, begin similar curriculum with them with goal of adolescent understanding all topics at age of transition.

General Information	Health Maintenance	Acute Episodes	Treatments	Psychosocial
o Introduction o Genetics o Growth & Development o Prognosis o Role of Primary and Specialty Care	o Penicillin o Immunizations o Nutrition o TCD Screening o Contraception o Hydration o Nocturnal Enuresis o Smoking o Pain Prevention o Anemia o Dental Care o Vision exams	o Access to Care o Fever o VOC and Home Management o Acute Chest o Splenic Sequestration o Aplastic Crisis o Stroke o Priapism o AVN o Gallstones o Leg Ulcers	o Blood Transfusions o Hydroxyurea o Chronic Transfusion o Bone Marrow Transplant	o Parenting a Child with a Chronic Illness o Child Care o Education and Educational Advocacy o Transition to Adult Care o Vocational Issues o Fears of Addiction o Chronic Pain o Drug and Alcohol Use o Depression and Anxiety

[1] Information on these topics may be found in the National Heart, Lung, and Blood Institute text *Management of Sickle Cell Disease*. See References.

IV. Laboratory Monitoring

CBC with reticulocyte count	Within first year of life and q year thereafter
Quantitative electrophoresis	Confirmation usually performed by newborn screening Repeat between 1 and 2 years of age Family studies and/or DNA-based testing if needed for clarifying diagnosis or genetic counseling
RBC antigen testing[2]	Between 1 and 2 years of age, or before first transfusion
LFTs/Bili/Renal	Annually
Urinalysis	Annually in older children and adolescents

V. Medications

A. Prophylactic Antibiotics[3]

- Standard of care is prophylaxis with penicillin VK from diagnosis.
- Penicillin VK (125 mg/5 mL, 250 mg/5 mL; 250 mg & 500 mg tablets).

Penicillin	Birth - 36months	125mg PO BID
Penicillin	3 y.o. - 5 y.o.	250mg PO BID
Penicillin	>5 y.o.	If surgically splenectomized continue 250 mg PO BID indefinitely, otherwise may discontinue.

- May use amoxicillin chewables if helpful to improve compliance at same dosing.
- May substitute tablets, unconstituted suspension (with diluent), amoxicillin chewables, or IM Bicillin for travel.
- Erythromycin ethyl succinate (200mg/5mL, 400mg/5mL; 400mg tablets) may be substituted for penicillin in patients with allergy; consider formal testing to determine if true allergy to penicillin or any other antibiotics.

Erythromycin ethyl succinate	Birth - 5 years and beyond if splenectomized	~20 mg/kg divided into BID dosing

- Consider IM Bicillin for patients with severely non-compliant families.

B Folic acid

- Not necessary for all patients with SCD.
- Generally recommended for patients with hemolytic anemia due to increased erythropoietic rate. However, increased supplementation of food supply in North America (cereal, grains, orange juice etc.) has made the need for further supplementation controversial.
- Required for:
  - Adolescent females (reproductive potential).
  - Pregnant patients.
- Strongly recommend for:
  - Patients with significantly elevated hemolysis (reticulocyte count >10%).
  - Reported diet low in enriched products and natural sources.
- Concern that increasing the numbers of medications given has a negative impact on overall medication compliance, especially for those taking more 'essential' prophylactic antibiotics and hydroxyurea.
- Risk of masking vitamin B_{12} deficiency has been reported.

[2] See the Clinical Practice Guideline on blood transfusions for information of RBC antigen testing.
[3] Some practitioners advocate keeping a supply of oral antibiotic 'on hand' for febrile episodes to be taken prior to seeking medical attention. This approach must be coupled with strong reinforcement that this is NOT a substitute for evaluation and parenteral treatment.

- May obtain 400mcg/day with OTC multivitamin, ensure iron is not added unless documented iron deficiency. Also available as 1 mg tablets with prescription.

C. Hydroxyurea

The careful selection of appropriate recipients, intensive family education, and monitoring of therapeutic effect and toxicity should be done under the direct care of a hematologist familiar with its use in pediatric patients.

VI. Screening[4]

Pulmonary Function Tests (PFTs)	SaO2 q visit Baseline PFT when ≥ 12 years • Consider repeating after severe or recurrent ACS • Repeat annually if persistent RAD or if previous year abnormal More extensive screening for those with pulmonary complications in childhood
EKG and echocardiogram	CXR, EKG and echo only if clinical concern including unusual murmur, hx of fluid intolerance or significant pulmonary disease. Lower threshold for cardiac evaluation in older adolescents.
Transcranial Doppler Ultrasound (TCD)[5]	q 6-12 months from ages 3 to 16 years. Not indicated in patients with HbSC or HbS-β^+ thalassemia, or those on chronic transfusion programs
Dilated ophthalmology with retinal exam	Annually once 10 years old
Neuropsychometric testing[6]	Consider for school or developmental concerns[7]
Audiology	Only if clinical concern, including the prolonged use of ototoxic antibiotics or meningitis
Abdominal ultrasound	Not appropriate as screening. Only if clinical concern

VII. Immunization

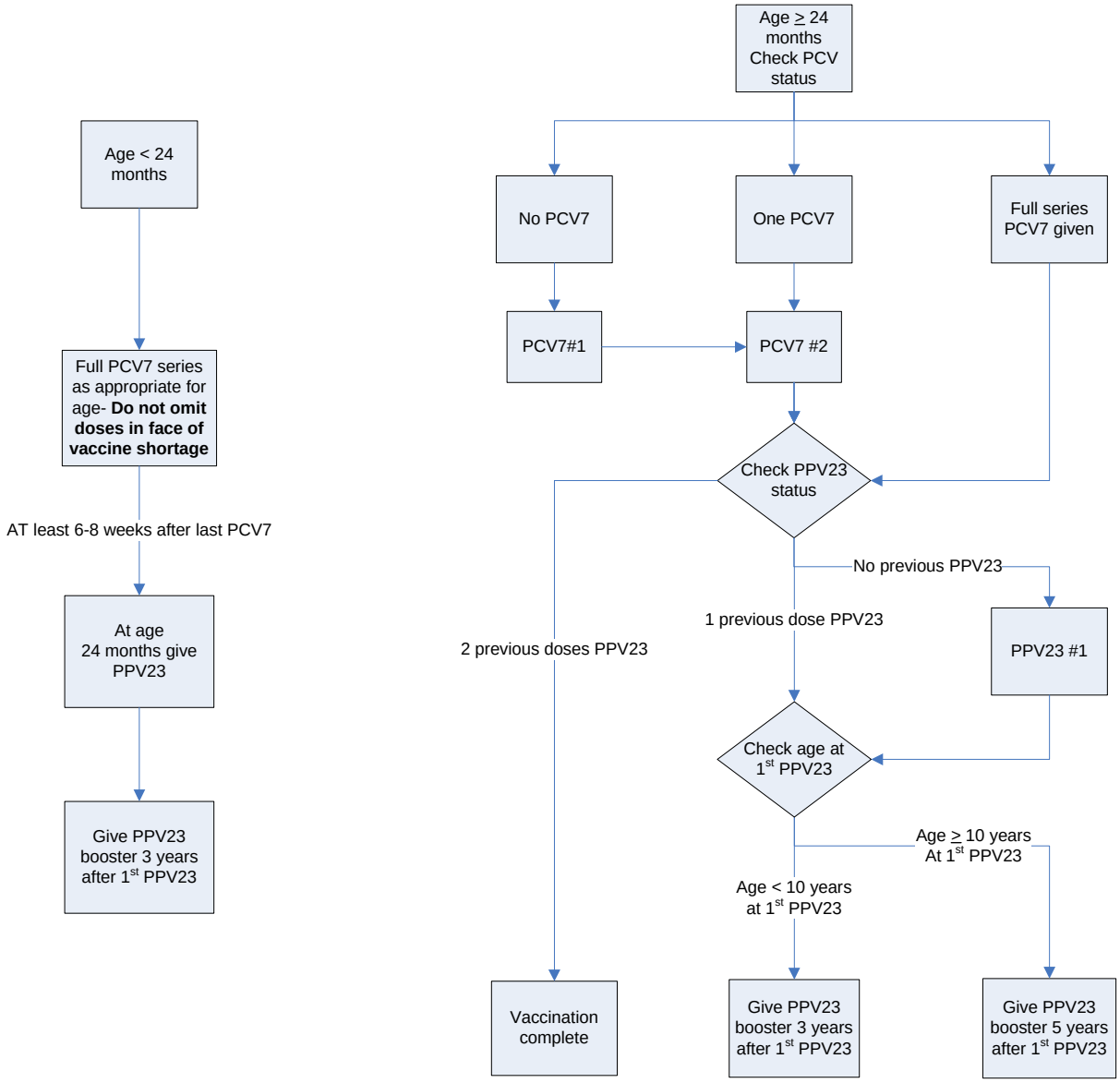
- Ensure patient is up-to-date with immunizations before surgical splenectomy, and consider administering booster doses if initial series were given more than 5 years ago.
- Ideally, all immunizations are given at least 6 weeks before surgical splenectomy.

A. Pneumococcal Immunizations

- Patients of all ages require coverage with both the conjugate (PCV7, Prevnar™) and the polysaccharide (PPV23, Pneumovax™) vaccines.
- For patients requiring both PCV7 and PPV23 they cannot be given at same visit. Give any PCV7 doses first, and then PPV23 at least 6-8 weeks after last PCV7.
- Children < 24 months should receive PCV7 as per childhood immunization schedule, then begin PPV23 series at age 24 months (see below).
- Children ≥ 24 months should receive PCV7 and PPV23 (see below).

[4] See the Clinical Practice Guideline on blood transfusions for the additional screening required for patients with iron overload.
[5] See the Clinical Practice Guideline on stroke for further information in evaluating patients for stroke risk.
[6] See the Clinical Practice Guideline on stroke for evaluation of patients with silent and overt CVA.
[7] Formal neuropsychometric testing is difficult to access in many centers. Also investigate assessment options within the early intervention and public school systems.

- During times of vaccine shortage infants with SCD should receive all 4 doses on schedule



** Adapted from NHLBI, Management of Sickle Cell Disease, June 2003*

B. Haemophilus influenza b (Hib)

- Hib as per routine childhood schedule.
- For ages over 5 and unimmunized, give 1-2 doses at least 1 month apart.

C. Meningococcal

- May be given after age 24 months.

- Should be given pre-splenectomy and before residential living (e.g. dorm).
- May need booster before residential living if it has been more than 5 years since initial vaccination.
- Recommended by AAP Red Book, but not standard in all hematology programs.
- Consider expanded use for other patients.

D. Influenza

- Inactivated, injectable vaccine to be given annually from age 6 months, ideally before December of each season.
- Recommend household contacts be vaccinated.
- Live intra-nasal vaccine (Flu-Mist™) is not currently recommended for patients with hemoglobinopathies.

Inactivated, Injectable Influenza Vaccine*

Age	Dose	Number of Doses
6-35 months	0.25 mL	1 or 2*
3-8 years	0.5 mL	1 or 2*
9 years to adult	0.5 mL	1

**CDC 2003-2004 recommendations*

- Two doses are recommended for children under 9 years of age who are receiving influenza vaccine for the first time. Administer at least one month apart and, if possible, give second dose before December.

E. Hepatitis A

- If Hepatitis C positive, chronically transfused, or before travel to country where prevalent.

F. Hepatitis B

- Ensure patient has received Hepatitis B series.

G. International Travel

- Consider additional vaccines before international travel.
- May consult Travel Medicine or www.cdc.gov for more information.

VIII. Pregnancy and Contraception

A. Counseling and Teaching

- Counsel that SCD does not impair fertility.
- Review the inheritance of sickle cell disease and trait, including the role of β-thalassemia and other abnormal hemoglobins.
- For females review pregnancy related complications and need for close pre-natal monitoring.

B. Hydroxyurea Patients

- Counsel patients and parents of minor patient re: possible teratogenic effects.
- Given the minimal data available regarding pregnancy outcomes for persons on hydroxyurea counsel both male and female patients to use effective methods of contraception if sexually active.
- Counsel male and female patients to discontinue treatment before planned pregnancy.
- Counsel female patients that if pregnancy is suspected to discontinue medication until tested for pregnancy.
- Many hematologists require use of hormonal contraception for female patients of reproductive age on hydroxyurea.

C. Contraception

- Estrogen containing contraceptives are not contraindicated in females with SCD in absence of other risk factors.
- Some evidence that injected progesterone-based contraceptives may ameliorate painful crises and be easier to comply with than daily pills.
- Counsel patients that a barrier method is necessary as an adjunct to hormonal methods to prevention HIV and other STDs.

D. Pregnancy

- Refer pregnant patients to high-risk OB experienced with the care of SCD.

E. Termination

- Therapeutic abortion with injection of hypertonic saline solution should be avoided as this may induce sickling.

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