Guidelines

For the Management of

Sickle Cell Disease

By

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Sickle cell anemia (SCA)
refers to the clinically similar disorders HbSS or HbSβ^0- thalassemia.
Sickle cell disease (SCD)
refers to all disease genotypes, including SCA and compound heterozygous disorders, such as HbSC, HbSD, and HbS β+-thalassemia**.**
The carrier state for hemoglobin S (HbAS or sickle cell trait) is not a form of SCD**.**

Typical Laboratory Findings in Sickle Cell Disease						
Genotype	**Hb (g/dL)**	**HbS (%)**	**HbA (%)**	**HbA_2 (%)**	**HbF (%)**	**HbC (%)**
SS	6–9	>90	0	<3.5	<10	0
$S\beta^0$-thalassemia	7–9	>80	0	>3.5	<20	0
$S\beta^+$-thalassemia	9–12	>60	10–30	>3.5	<20	0
SC	9–14	50	0	<3.5	≤1.0	45
Typical Laboratory Findings in Sickle Cell Trait						
AS	normal	≤40	>60	<3.5	≤1.0	0

•Hb = hemoglobin; HbS = sickle hemoglobin; HbA = normal adult hemoglobin;
HbA_2 = minor variant of adult hemoglobin; HbF = fetal hemoglobin;
HbC = hemoglobin variant that causes manifestations of SCD when paired with HbS
•The hemoglobin values in this exhibit apply in the absence of a blood transfusion in the last 4 months, are not absolute, and are applicable to adults and children only (not newborns).

Prevention of Invasive Pneumococcal Infection
Young children with SCA have a very high risk for septicemia and meningitis in the absence of appropriate prophylaxis however; those with HbSC and HbS β^+-thalassemia have a much lower incidence of life-threatening infection because their spleen function is normal or only minimally impaired during infancy.
Older children and adults with all SCD genotypes are at increased risk for invasive bacterial infection.
The prevention strategy involves:
1. Assure that people of all ages with SCD have been vaccinated against S. pneumoniae and other encapsulated pathogens
2. Administer oral penicillin prophylaxis (125 mg for age <3 years & 250 mg for age ≥3 years) twice daily until age 5 in all children with HbSS.
Discontinue prophylactic penicillin in children with HbSS at age 5 unless they have had a splenectomy or invasive pneumococcal infection. When discontinuing penicillin prophylaxis at age 5, it is important to assure that the child has completed the recommended pneumococcal vaccination series, and if not, complete the series immediately.
4. Consider withholding penicillin prophylaxis from children with HbSC disease and HbS β^+-thalassemia unless they have had a splenectomy.
5. Educate those with SCD to seek immediate medical attention in the event of fever.

Screening for Renal Disease
Renal abnormalities can start with defects in urine concentration and acidification beginning in childhood and progress with age to microalbuminuria, overt proteinuria, glomerulosclerosis, and, in some people, renal failure.
Screen all individuals with SCD, beginning by age 10, for proteinuria.
If the result is negative; repeat screening annually.
If the result is positive, perform a first morning void urine albumin-creatinine ratio.

Screening for Hypertension
In adults with SCD, screen for hypertension is indicated with target treatment to lower blood pressure ≤140/90

Screening for Pulmonary Hypertension PH
Pulmonary hypertension (PH) is defined as an elevation of the resting mean pulmonary arterial pressure (≥25 mmHg) as determined by right heart catheterization.
There are several potential etiologies for elevation in mean pulmonary artery pressure in people with SCD.
1. Chronic hemolytic anemias, including SCD, may result in pulmonary vascular changes leading to pulmonary arterial hypertension (PAH), and are placed in Group 1 of the current classification. (*World Health Organization (WHO) clinical classification system)*
2. The second type of PH in SCD is pulmonary venous hypertension (PVH), which is assigned to Group 2 in the current classification and is associated with an elevated mean pulmonary artery pressure ≥25 mmHg but also an elevated pulmonary capillary wedge pressure of ≥15 mmHg.
3. PH also occurs in the setting of chronic lung disease, chronic thromboembolic disease, or can be due to unclear or multiple mechanisms (Groups 3, 4, 5 respectively).
Screening to detect PH in the pre-symptomatic stage is justified to prevent or reduce morbidity and/or mortality. The main symptoms of PH include shortness of breath during routine activity, such as climbing two flights of stairs; fatigue; lethargy; chest pain; palpitations; syncope; peripheral edema; and decreased appetite.
However; there is no indication for routine screening with resting electrocardiography, exercise treadmill test or CT scanning for coronary calcium for the presence of severe coronary artery stenosis (CAS) or the prediction of coronary heart disease (CHD) events in adults at low risk for CHD events. No consistent results documented efficacy of bosentan, sildenafil, L-arginine, L-carnitine, hydroxyurea as treatment option for pulmonary hypertension

Screening for Pulmonary Disease
Children and adults with SCD found to have signs or symptoms of respiratory problems by history and/or physical examination need assessment including pulmonary function tests.
No indication of screening asymptomatic children and adults with pulmonary function test

Screening for Retinopathy
All individuals with SCD and especially those with HbSC are at risk for retinal disease due to vaso-occlusion and its resultant ischemia leading to proliferative sickle retinopathy (PSR: the development of sea-fan-shaped neovascular fronds in response to local ischemia) which is associated with loss of visual acuity, vitreous hemorrhage and retinal detachment.
The onset of sickle retinopathy is in childhood; therefore; screen for retinopathy beginning at age 10. Those having a normal dilated retinal examination, re-screen at 1–2 year intervals.

Screening for Risk of Stroke

Stroke is one of the most common and devastating complications of SCD. In the absence of primary stroke prevention, approximately 10 % of children with SCA will have overt stroke which is secondary to stenosis or occlusion of the internal carotid or middle cerebral artery. Trans-cranial Doppler (TCD) imaging of large intracranial blood vessels (to detect increased velocities secondary to stenosis) can predict risk of stroke in children with SCA; however; TCD is not predictive of stroke risk in adults as in children.

TCD reading is the time averaged mean maximal cerebral blood flow velocity

• In children with SCA, screen annually with TCD beginning at age 2 until at least age 16. Children with conditional (170–199 cm/sec) or elevated (>200 cm/sec) TCD results, arrange chronic transfusion therapy aimed to primary stroke prevention.

• No indication for screening with TCD in children with genotypes other than SCA (e.g., HbS β^+-thalassemia or HbSC).

• No indication for screening with MRI or CT in asymptomatic children or adults with SCD

Contraception & conception

There is no evidence that intrauterine devices IUDs pose an increased risk for women with SCD. Hormonal contraceptives may decrease menstrual blood flow, leading to higher hemoglobin levels. If the benefits are considered to outweigh the risks, combined hormonal contraceptives (pills, patches, and rings) may be used in women with SCD, however; history of stroke is a contraindication to combined hormonal contraception.

The use of progestin-only hormonal contraceptives lowers the risk of thromboembolism compared to use of estrogen-containing contraceptives and has been shown to be safe for women with SCD. Progestin-only contraceptives were not associated with an increased risk of thrombosis and may have non-contraceptive benefits in terms of fewer crises and improved hematologic parameters.

Progestin-only contraceptives (pills, injections, and implants), levonorgestrel IUDs and barrier methods have no restrictions or concerns for use in women with SCD.

After spontaneous conception, prenatal diagnosis of SCD is possible by chorionic villus sampling in the first trimester or by amniocentesis in the second trimester of gestation. Pregnancy in women with SCD is considered high risk, and there is an increased risk of adverse pregnancy outcomes including fetal (intrauterine) growth restriction, preterm delivery, and stillbirth.

During pregnancy, these are increased frequency of pain crises, risk of thrombosis, infections, preeclampsia, and death relative to women who do not have SCD.

For newborns arrange:

***** SCD screening with clinical consideration of confirmatory test within 2 months

* Hypothyroidism screening
* Hearing loss screening
* Phenylketonuria (PKU) screening
* Prophylactic ocular topical medication for the prevention of gonococcal ophthalmia neonatorum

For children (aged 3 months to 12 years or as stated) arrange:

* Fluoride supplement in those ≥ 6 months of age whose water supply is deficient in fluoride
* Routine iron supplementation for asymptomatic infants aged 6-12 months who are at increased risk for iron deficiency anemia
* Children aged 3-5 years should receive routine ophthalmological evaluation

For adults arrange:
* Virus screening for Hepatitis B, C & HIV especially those with multiple transfusions
* Screen for obesity
* Screen women for gynecological infection
* Screen for cervical & breast cancer in women ages 21-65 years
* Folic acid supplementation whenever considering pregnancy to prevent neural tube defects
* Cardiovascular disease risk screening especially those at risk

Immunizations
Because of their increased susceptibility to invasive pneumococcal & other encapsulated organisms, the following immunizations are of special importance to people with SCD:
All infants with SCD
– Should receive the complete series of the 13-valent conjugate pneumococcal vaccine series beginning shortly after birth and then the 23-valent pneumococcal polysaccharide vaccine at age 2 years with a second dose at age 5 years.
Pneumococcal (PCV13) vaccine—Children
– Aged 6-18 years with functional or anatomic asplenia should receive one dose of PCV13.
Pneumococcal vaccine-native Adults
– Adults aged ≥19 years with functional or anatomic asplenia who have not previously received PCV13 or PPSV23 should receive
• One dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later.
• Subsequent doses of PPSV23 should follow current PPSV23 recommendations for adults at high risk.
– A second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years with functional or anatomic asplenia.
– Additionally, those who received PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later if at least 5 years have elapsed since their previous PPSV23 dose.
Previous vaccination with PPSV23—Adults
– Adults ≥19 years with functional or anatomic asplenia who have received ≥1 dose of PPSV23 should be given a PCV13 dose ≥1 year after the last PPSV23 dosed.
– For those who require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after PCV13 and at least 5 years after the most recent dose of PPSV23.
Hib (Haemophilus influenzae type B) vaccine
– One dose of Hib vaccine for people aged >5 years who have SCD if they have not previously received Hib vaccine
Meningococcal vaccine
– Vaccinate infants at high risk (including those with SCD) at 2, 4, 6 months of age and again at 12 -15 months with this vaccine, which is generically known as HibMenCY.
– Persons aged 9 months - 55 years at increased risk for meningococcal disease (e.g., adults with anatomic or functional asplenia or persistent complement component deficiencies) should receive MenACWY.
– Children aged 2 months - 6 years should receive an additional dose of MenACWY 3 years after primary immunization; boosters should be repeated every 5 years thereafter.
– Children ≥7 years of age should receive an additional dose of MenACWY 5 years after primary immunization; boosters should be repeated every 5 years thereafter.

Acute Complications of Sickle Cell Disease

Acute vaso-occlusive crisis (VOC), fever related to infection, acute kidney injury (AKI), hepatobiliary complications, acute anemia, aplastic crisis, splenic sequestration, acute chest syndrome (ACS) and acute stroke.

Priapism and acute ocular conditions such as central retinal artery occlusion (CRAO) also require urgent management to preserve organ function.

Vaso-Occlusive Crisis VOC

A VOC is the most common acute complication for persons with SCD and defined as pain resulting from tissue ischemia caused by vaso-occlusion most commonly in the bone(s) and bone marrow.

VOCs are typically associated with excruciating pain of sudden onset but some people experience gradual onset of a VOC. VOCs and their accompanying pain most commonly occur in the extremities, chest, and back.

Nearly all individuals affected by SCD will experience a VOC during their lifetime with the first VOC may occur as early as 6 months of age, often presenting as dactylitis, but thereafter VOCs occur with variable frequency.

There are no tests to rule in or to rule out a VOC; but potentially rule out other causes of pain.

Persons with the genotypes HbSS or HbS β^0-thalassemia are likely to experience more frequent VOCs. *Those with HbAS (sickle cell trait) do not experience typical VOCs*.

The primary management of a VOC is analgesic with/out opioids, hydration, non-pharmacologic therapy (local heat application and distraction) & concurrent treatment of itching caused by histamine release especially if opiates used.

For patients with mild to moderate pain & patient reports relief with NSAIDS in the absence of contraindications, continue treatment with NSAIDS.

For severe pain, rapidly initiate treatment with parenteral opioids. Reassess pain and re-administer opioids if necessary every 15–30 minutes until pain is under control.

Administer oxygen if oxygen saturation <95 % on room air.

Before discharge, wean parenteral opioids prior to conversion to oral opioids and adjust home dose of opioid prescriptions to prevent opioid withdrawal after discharge.

Those who require antihistamines for itching secondary to opioid administration, prescribe agents orally and do not re-administer with each dose of opioid but re-administer every 4- 6 hours if needed. Blood transfusion is not indicated for VOC per se

Fever

The increased risk of severe bacterial infection results primarily from reduced or absent splenic function usually after 2 or 3 months of age, as fetal hemoglobin HbF declines, infants with SCA begin to develop splenic impairment resulting to extremely high risk of septicemia and meningitis, primarily due to Streptococcus pneumoniae.

The risk of such infections continues throughout childhood and to a lesser extent in adults.

Serious infections can also affect other forms of SCD (HbSC, HbS β^+-thalassemia).

Fever associated with pain should not be considered a VOC until infection is ruled out.

Parvovirus B19 may be responsible for the development of apalstic crisis, stroke and acute chest syndrome ACS.

Patient with temperature ≥101.3°F (38.5°C), immediately evaluate with history, physical examination, complete blood count (CBC), reticulocyte count, blood & urine culture.

Promptly administer ongoing empiric parenteral antibiotics that cover S. pneumoniae and gram-negative enteric organisms pending results of investigations.

Patient who have localized or multifocal bone tenderness, especially when accompanied by erythema and swelling include bacterial osteomyelitis in the differential diagnosis and manage accordingly
Initial empiric therapy include cefotaxime (225-300 mg/kg/d divided every every 8 h) or ceftriaxone (100 mg/kg/d divided every 12-24 h) along with vancomycin (60 mg/kg/d divided every 6 h). Meropenem may be an alternative to ceftriaxone in a dose of 40 mg/kg IV q8hr; not to exceed 2 g IV q8hr.

Acute Renal Failure ARF
The most common renal complication in people with SCD is hyposthenuria (inability to concentrate the urine), also albuminuria and papillary nicrosis.
Initiate ACE inhibitor therapy if microalbuminuria is documented
ARF may be due to renal papillary necrosis due to medullary infarction from obstruction of the blood supply in the vasa recta and presents with flank pain and hematuria. Associated fever suggests super-infection.
ARF may also occur when individuals with chronic sickle cell nephropathy or other chronic kidney diseases are exposed to dehydtation or to nephrotoxic medications (NSAIDs or IV contrast dye).
The inability to maximally concentrate the urine may result in increased vulnerability to pre-renal azotemia.
Due to increased renal tubular secretion of creatinine, serum creatinine values in SCD do not rise until significant renal impairment occurs (GFR of 30 mL/min or less). Since the serum creatinine levels are generally low or low-normal in individuals with SCD, the values in ARF may still be within normal limits even if they have doubled from baseline.
Acute and chronic renal replacement therapy, including hemodialysis, is well-tolerated by people with SCD and should be used when indicated.
ARF may respond to exchange red blood cell transfusion when associated with acute multisystem organ failure MSOF attributed to diffuse vaso-occlusion. However, the benefit of transfusion for other causes of ARF in SCD has not been confirmed.

Priapism
Priapism is a sustained, unwanted painful erection lasting 4 or more hours.
Stuttering priapism is the occurrence of multiple self-limited episodes of shorter duration (<4 hours) and can be a harbinger of sustained events.
Priapism is usually of the low flow ischemic type and characterized by pain and a soft glans.
Prompt recognition of priapism and initiation of conservative medical management may lead to detumescence and limit the need for more aggressive and invasive intervention as delayed diagnosis and therapy can result in impotence. These managements include vigorous oral or intravenous hydration and oral or intravenous analgesia and consultation with a urologist.
Do not use transfusion therapy for immediate treatment of priapism associated with SCD but might be needed if surgical intervention is required.

Cholelithiasis and Acute Cholecystitis
Gallstones are usually asymptomatic but can be associated with acute infection and inflammation involving the gallbladder. Acute cholecystitis can occur with or without the presence of gallstones

Sickle cell hepatopathy
Include acute hepatic sequestration (AHS) and acute intrahepatic cholestasis (AIC).
AHS is marked by hepatic enlargement compared to baseline with ≥ 2 g/dL decline in hemoglobin concentration. Sequestration of red blood cells often develops over a few hours to a few days, and the resultant stretching of the hepatic capsule is usually painful with hepatomegally & mild elevations of liver function tests.
AIC is characterized by the sudden onset of right upper quadrant pain, increasing jaundice, progressively enlarging and tender liver, light-colored stools, extreme hyperbilirubinemia (both conjugated and unconjugated usually without urobilinogenuria) hypoalbuminemia, thrombocytopenia & coagulation abnormalities.
The clinical picture suggests cholestatic jaundice or choledocholithiasis but without evidence of common duct obstruction or cholangitis. AIC may be fatal if not treated promptly.
Treatment of of AHS or AIC include hydration, rest, correct heamatological abnormalities and simple or exchange transfusion.

Acute Anemia
Nearly all people with SCD have chronic anemia but individual baseline hemoglobin values vary widely depending upon hemoglobin genotype, current and recent therapies (blood transfusions and hydroxyurea in particular).
Baseline values are typically 6–8 g/dL for people with SCA, 10–15 g/dL for people with HbSC, and 9–12 g/dL for people with HbS β^+-thalassemia.
Acute anemia, defined as a decline by ≥2.0 g/dL in hemoglobin concentration below the patient's baseline value, can be due to splenic sequestration in a child or an aplastic episode at any age and may require urgent evaluation and therapy.
During acute events, the reticulocyte count is an important addition to the CBC to assess whether the acute anaemia is due to diminished red blood cell production (low reticulocyte count, as can occur in parvovirus infection resulting in aplastic crisis), or accelerated hemolysis, or sequestration in the lungs, spleen, or liver (high reticulocyte count).

Aplastic Episode
An aplastic episode or "crisis" is a common feature, especially in children with HbSS.
The usual clinical picture is gradual onset of fatigue, shortness of breath, and sometimes syncope. Fever is quite common as well.
The hemoglobin value (typically 3–6 g/dL) is usually far below the person's baseline level, and the reticulocyte count is reduced or even zero.
It has been noted that people with SCD rarely have recurrences of aplastic crisis suggesting an infectious etiology mostly parvovirus B19 which destroys erythroid precursors in the bone marrow, so people with an extremely short red blood cell lifespan such as those with SCA are susceptible to rapid decline in their hemoglobin concentration.
Resolution of the aplastic crisis is heralded by marked reticulocytosis and rising hemoglobin concentration. The resulting humoral immunity is life long, preventing recurrent events.

Splenic Sequestration
Defined as sudden enlargement of the spleen and reduction in hemoglobin concentration by at least 2 g/dL below the baseline value with elevated reticulocyte count and circulating nucleated red blood cells, the platelet count is generally decreased because both red cells and platelets are trapped in the spleen.
It may occur as early as several months of age although it is more typical between 1-4 years old as involution & auto-infarction of the spleen occurs by age 5 especially in HbSS patients. In older people, it may occur more insidiously.

Treatment consists of IV fluid resuscitation for hypovolaemia, blood transfusion aimed at partial correction of the anemia; excessive transfusion (to hemoglobin values over 8 g/dL) should be avoided as the sequestered erythrocytes in the enlarged spleen typically reenter the circulation several days later leading to hyperviscosity due to an excessively high hemoglobin concentration.
People with recurrent sequestration, a single life-threatening acute sequestration or symptomatic hypersplenism are indicated for splenectomy.
Splenectomy for splenic sequestration does not further increase the risk of death or bacteremia since most patients are already functionally asplenic.

Acute Chest Syndrome ACS
ACS is one of the most common and serious acute complications of SCD. It is the second most frequent reason for hospitalization and the most common cause of death.
Clinically, ACS resembles pneumonia and can develop suddenly or insidiously, during hospitalization for a VOC, or after a surgical procedure,
Children usually have fever and upper or middle lobe involvement, whereas adults are often afebrile and present with multi-lobe disease.
The most common etiology is infection but the complication may also result from bone marrow fat embolism, intrapulmonary aggregates of sickled cells, atelectasis, or pulmonary edema.
There are no distinctive laboratory features of ACS, although the hemoglobin concentration often declines sharply below the patient's baseline value.
Treatment of ACS may include IV cephalosporin, an oral macrolide, oxygen, bronchodilators, and blood transfusions to those with hemoglobin concentration is >1.0 g/dL below baseline
Urgent exchange transfusion is indicated when there is rapid progression of ACS manifested by oxygen saturation < 90% despite supplemental oxygen, increasing respiratory distress and progressive pulmonary infiltrates, and/or decline in hemoglobin concentration despite simple transfusion

Acute Stroke
Stroke is one of the most common and devastating complications of SCD presents as neuorological deficit, seizures or coma and results in adverse motor and cognitive sequelae.
Transient ischemic attack may precede stroke, even in children, but neuro-imaging is negative and not predictive of stroke.
Overt stroke is generally secondary to stenosis or occlusion of the internal carotid or middle cerebral artery, the events may be precipitated by ACS, parvovirus infection or other acute anemic events.
There is high recurrence rate in the absence of secondary prevention measures such as a chronic transfusion program or hematopoietic stem cell transplantation.
Adults with HbSS also have a high risk of both ischemic and hemorrhagic stroke.
Perform regular blood transfusions as primary stroke prevention in children with high risk of stroke screened by transcranial Doppler TCD.
Initiate a program of monthly simple or exchange transfusions in patients who have had a stroke if it is not possible to implement a transfusion program, initiate hydroxyurea therapy.

Multisystem Organ Failure
Multisystem organ failure (MSOF) is a severe and life-threatening complication usually associated with a VOC and characterized by failure of the lungs, liver, kidneys, fever, rapid decline in hemoglobin concentration and platelet count, and non-focal encephalopathy.

MSOF may occur after several days of hospitalization and treatment for a severe VOC, often when pain is beginning to improve.
Patient with SCD and MSOF, immediately initiate simple or exchange transfusion, respiratory support and renal replacement therapy when needed for acute renal failure

Acute Ocular Conditions
In persons with SCD, acute ocular complications manifested by occlusion of the eye vasculature or progression of proliferative sickle retinopathy (PSR), hyphema, central retinal artery occlusion (CRAO), orbital and periorbital infections, orbital infarction, and orbital compression syndrome (OCS) which all requires urgent assessment and therapy.

Chronic Pain
In SCD, pain is considered chronic if it lasts more than 3 months.
The major types of SCD-associated chronic pain include the following:
• Chronic pain often of unclear etiology. This type of chronic sickle cell pain may be an extension of recurrent acute painful episodes.
• Chronic pain in a specific tissue or organ, such as avascular necrosis (AVN) of the hips, or leg ulcers.
• Chronic neuropathic pain. This is usually described as burning, numb, tingling, lancinating, shooting, or paroxysmal in nature and is associated with a sensation of pins and needles. Its severity is also enhanced by exposure to either cold or heat.
• "Breakthrough" pain often identified by health care professionals who treat the patients
Medications used to treat SCD-related pain should be tailored to the individual & include NSAIDs, opioids, antidepressants, and anticonvulsant medications. This may be enhanced by adding non-pharmacologic approaches including psychological intervention, occupational therapy, behavioral and cognitive interventions, acupuncture, mild to moderate exercise and aqua therapy.

Hydroxyurea
This drug; besides other mechanisms; can increase HbF levels & improve clinical outcomes, especially pain and ACS. The benefit effect is mostly seen in people with SCD genotypes HbSS or HbS β^0-thalassemia.
Treatment with hydroxyurea is indicated in:
- Adults with SCA who have three or more sickle cell-associated moderate to severe pain crises in a 12-month period or any sickle genotype who have sickle cell-associated pain that interferes with daily activities and quality of life,
- Adults with SCA who have a history of severe and/or recurrent ACS,
- Adults with SCA who have severe symptomatic chronic anemia that interferes with daily activities or quality of life,
- Infants 9 months of age and older, children, and adolescents with SCA regardless of clinical severity to reduce SCD-related complications (e.g. pain, dactylitis, ACS, anemia).
- Adults and children with SCD who have chronic kidney disease and are taking erythropoietin, hydroxyurea therapy can be added to improve anemia.
* In females who are pregnant or breastfeeding, discontinue hydroxyurea therapy.
* Encourages shared decision making of hydroxyurea therapy with all patients.
The following laboratory tests are recommended before starting hydroxyurea:
• Complete blood count (CBC) & differential,
• Metabolic profile, including renal and liver function tests
• Pregnancy test for women
• Quantitative measurement of HbF if available

Initiating and Monitoring Therapy

• Baseline elevation of HbF should not affect the decision to initiate hydroxyurea therapy.
• Both males and females of reproductive age should be counseled regarding the need for contraception while taking hydroxyurea.
• Starting dosage of hydroxyurea:
- for adults is 15 mg/kg/day;
-for patient with chronic kidney disease 5–10 mg/kg/day;
- for infants and children 20 mg/kg/day:
• Monitor CBC & differential every 4 weeks with aim for a target platelet count ≥80,000/uL; absolute neutrophil count ≥2,000/uL; however, younger patients with lower baseline counts may safely tolerate absolute neutrophil counts down to 1,250/uL.
• If neutropenia or thrombocytopenia occurs:
– Hold hydroxyurea dosing
– Monitor CBC with differential weekly
– When blood counts have recovered, reinstitute hydroxyurea at a dose 5 mg/kg/day lower than the dose given before onset of cytopenias
• If dose escalation is warranted, proceed as follows:
– Increase dose of hydroxyurea by 5 mg/kg/day increments every 8 weeks
– Give until mild myelosuppression (absolute neutrophil count 2,000/uL to 4,000/uL) is achieved, up to a maximum of 35 mg/kg/day.
• Once a stable dose is established, monitoring every 2–3 months
• People should be reminded that the effectiveness of hydroxyurea depends on their adherence to daily dosing & not to double up doses if a dose is missed.
• A clinical response to treatment with hydroxyurea may take 3–6 months; therefore, a 6- month trial on the maximum tolerated dose is required prior to considering discontinuation due to treatment failure, whether due to lack of adherence or failure to respond to therapy.
• Monitor RBC MCV and HbF levels for evidence of consistent or progressive laboratory response. A lack of increase in MCV and/or HbF is not an indication to discontinue therapy.
• For the patient who has a clinical response, long-term hydroxyurea therapy is indicated.
• Hydroxyurea therapy should be continued during hospitalizations or illness.

Blood transfusion

In the form of simple transfusion or as an exchange transfusion. Benefits of exchange transfusion related to the removal of recipient sickle erythrocytes:
(1) Increasing the percent of normal (donor) hemoglobin (HbA)-containing erythrocytes remaining after transfusion;
(2) Permitting transfusion of increased volumes of donor blood without increasing the hematocrit to levels that excessively increase blood viscosity;
(3) Reducing the net transfused volume, this reduces iron overload
However, potential risks of exchange transfusion include:
(1) Increased donor unit exposure and subsequent alloimmunization;
(2) Higher costs;
(3) Need for specialized equipment;
(4) Need for permanent venous access.

Indications of blood transfusion:

1. *Prophylactic Perioperative Transfusion*

Used in the perioperative period to prevent the development of vaso-occlusive crises (VOCs),

stroke or ACS after surgery aiming to bring the hemoglobin level to 10 g/dL prior a surgical procedure involving general anesthesia.

2. Acute complications:

•Stroke
•Symptomatic acute chest syndrome combined with a decreased Hb of 1 g/dL below baseline
•Symptomatic severe ACS (defined by O_2 saturation ≤ 90% despite supplemental oxygen)
•Aplastic crisis
•Acute splenic sequestration plus severe anemia
•Hepatic sequestration or Intrahepatic cholestasis
•Multisystem organ failure (MSOF)
•Symptomatic anemia

3. Chronic transfusion program

With the goal to keep HbS level of < 30% immediately prior to next transfusion. Indicated in:
• Adults and children with previous clinically overt stroke
• Child with transcranial Doppler (TCD) reading >200 cm/sec

No indication of blood transfusion in:

Uncomplicated painful crisis
Priapism
Asymptomatic anemia
Acute kidney injury, unless multisystem organ failure (MSOF)

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