

BaselineEvaluation; Blood counts, red cell indices, percent Hb F, serum chemistry, pregnancy test. *Initiation of treatment*; Hydroxyurea, 10-15 mg/kg/day in a single daily dose for 6-8 weeks; CBC every 2 weeks; percent Hb F every 6-8 weeks; serum chemistry every 2-4 weeks. If no major toxicity, escalate dose by 2.5-5mg/kg every 6-8 weeks until the desired endpoint is reached to a maximum of 35mg/kg/day. Granulocytes should be $\geq 2,500/\mu\text{L}$, platelets $\geq 95,000/\mu\text{L}$. *Treatment Endpoint*; Less pain, increase in Hb F to 15-20 percent, increased hemoglobin level if severely anemic, improved well-being, acceptable myelotoxicity. Consider biological inability to respond to treatment or poor compliance with treatment if there is failure of Hb F (or MCV) to increase.

Preventive measures: Parent/Caregiver should be educated for;

- How to palpate spleen.
- Avoidance of vasoocclusive crises; avoidance of physical stress, infection, dehydration, hypoxia, cold swimming for prolonged periods, alcohol & advise adequate rest during menstruation.
- How to manage pain.
- Immunization: In addition to routine pneumococcal vaccine, PPV23 at 2 years and booster at 5 years.
- Prophylactic antibiotics: Oral penicillin VK until 5 years; preferably lifelong.
- Folic acid supplementation.
- Frequent visits-initially every 1-2weeks till stabilization of condition, thereafter every 2-6 months depending on patient phenotype and active problems.

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Reference: a) *Harrison textbook of internal medicine Edition 18th*
b) *Nelson textbook of pediatrics, Edition 19th, 1663-1671*
c) *The management of sickle cell disease. National Institute of Health. Division of blood disease and resources. http://www.nhlbi.nih.gov/files/docs/guidelines/sc_mngt.pdf*
d) *Steinberg MH. Management of sickle cell disease. N Engl J Med 1999;340:1021-30.* e) *Charache S, Terrin ML, Moore RD, et al. Multicenter Study of Hydroxyurea in Sickle Cell Anemia. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. N Engl J Med 1995;332:1317-22.*

Practical Guidelines for Management of Sickle cell disease

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History & Examination: Characteristic of pain episodes; frequency, duration, usual home treatment, average no./duration of hospitalizations, past medical treatment, surgery, transfusion, cerebrovascular events, liver/renal/bone/GIT/respiratory/eye complications, anemia, splenic pain, ophthalmologic evaluation for retinopathy. Family history; sickle cell, hypertension, diabetes, cancer, immunization history, medications and allergy.

Investigation: Complete blood count with GBP, reticulocyte count, red cell indices, sickling test, LDH, Hemoglobin Electrophoresis /HPLC, bone marrow (in Aplastic crisis), blood culture, liver function tests, renal function tests, s.ferritin, HBV/HCV/HIV tests, urine exam, chest X-ray, X-ray of involved site, USG abdomen, Bone scan, NCCT head/MRI(DWI)/MR venography.

Diagnosis: Sickle cell trait (Hb AS), Sickle cell disease (SCD): SCD-SS, SCD-S β^0/β^+ thal, SCD S α^0/α^+ thal, SCD-SC, SCD- SE, SCD- S $\delta\beta$ thal, S HBFH

Treatment:

- 1. Fever/Bacteremia:** (Medical emergency) Admission criteria (factors associated with high risk of bacteremia)- Hypotension, CRT > 4sec, Temp. > 40° C, WBC > 30,000/mm³ or < 500/mm³, PC < 1 lakh/mm³, H/o pneumococcal sepsis, severe pain, Hb < 5g/dl, dehydration, infiltration of lungs. Blood culture, i.v antibiotics: 3rd generation cephalosporin.
- 2. Dactylitis:** Pain medication (acetaminophen with codeine). Differentiate from osteomyelitis.
- 3. Splenic sequestration:** Clinical findings: Increase in spleen size, hypovolemia, Hb decline \geq 2g/dl from baseline Hb, reticulocytosis, \downarrow in Platelet count. IVF, 5ml/kg of PRBC (if required), Prophylactic splenectomy performed after an acute episode.
- 4. Pain:** Majority of painful episodes managed at home with heating blankets, relaxation techniques and massage. Early in course: acetaminophen/NSAIDs, if pain severe- Codeine (with aspirin or acetaminophen) 0.5-1 mg/kg every 3-4h oral. Morphine: i.v- 0.1-0.15mg/kg; oral- 0.3mg/kg every 3-4hrs, Ketorolac 30-60 mg, Hydroxyurea in adults \geq 3 painful episodes/year & in children with multiple painful episodes
- 5. Priapism:** Sitz bath, pain medication, if pain lasts > 4 hrs-aspiration of blood from corpora cavernosa followed by irrigation with dilute epinephrine.

- 6. Neurologic complications:** Overt stroke:- CT Head, if available-MRI(DWI), MR Venography. Oxygen (maintain spO₂ > 90%), simple blood transfusion to maintain Hb to maximum of 10g/dl & exchange transfusion (manually or erythrocytapheresis) to reduce Hb S < 50% or ideally < 30%.
- 7. Lung disease (Acute chest syndrome):** Blood culture, chest X-ray, oxygen, blood transfusion (simple or exchange), empirical antibiotic- cephalosporin and macrolide
- 8. Renal disease:** *Gross hematuria*; requires bed rest, increased fluid intake and if blood loss, iron replacement/blood transfusion. Thorough evaluation of hematuria is required. In *Acute renal failure*; transfusion/exchange transfusion. *Glomerular nephropathy/chronic renal disease*; no proven treatment, for asymptomatic proteinuria- ACE inhibitors, avoid NSAIDs, control BP, cautious use of diuretics, treat UTI vigorously.
- 9. Osteomyelitis:** Acute osteomyelitis must be differentiated from acute bone infarction. Radiographs rarely reveal bone changes early on. Marrow scan advised. Surgical drainage is the primary treatment. I.V therapy with antibiotics (according to sensitivity of organism) should be given for 2-6 weeks according to nature & extent of disease.

Special situations:

- Surgery/Anesthesia:** Achieve hemoglobin upto 10g/dl by simple/exchange transfusion. Pre-op; monitoring for hydration, hematocrit, peripheral perfusion & oxygenation status. Intra-op; monitor BP, pO₂, ECG. Post-op; monitor hydration, oxygen & respiratory therapy.
- Obstretical:** Contraceptives (oral) not contraindicated, patient should stop hydroxyurea if planning for pregnancy, close observation for preeclampsia, maintain hemoglobin up to 9g/dl with or without transfusion, hypertonic sodium chloride should not be used in interruption of pregnancy as it increases sickling.

Hydroxyurea: Indications; Adults, adolescents, or children with frequent pain episodes, history of acute chest syndrome, other severe vaso-occlusive events, or severe symptomatic anemia.