

**UNITED REPUBLIC OF TANZANIA**



**MINISTRY OF HEALTH**

**SICKLE CELL DISEASE  
CLINICAL MANAGEMENT  
GUIDELINES**



**JULY 2023**

**THE UNITED REPUBLIC OF TANZANIA**



**MINISTRY OF HEALTH**

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# **SICKLE CELL DISEASE CLINICAL MANAGEMENT GUIDELINE**

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**JULY 2023**

## FOREWORD

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It is my great pleasure to introduce the second edition of the Sickle Cell Disease (SCD) Management Guidelines. Sickle Cell Disease (SCD) is major health problem in Tanzania. Every year, approximately 14000 babies are born with SCD, and this number is expected to double by the year 2050. Tanzania has the fourth greatest number of annual SCD births in all of Africa, and the fifth greatest in the world. In addition, almost 20% of the Tanzanian population carries a copy of the sickle gene in a form of sickle cell trait (AS). The first edition of these guidelines was published over five years ago and since then; there have been significant advances in the understanding and management of SCD.

This second edition is the result of collaboration among experts in the field of SCD from around Tanzania. It provides a comprehensive update on the latest evidence-based recommendations for the management of SCD, including new information on diagnosis, treatment, and long-term care. The guidelines are designed to assist healthcare professionals in the care of patients with SCD and to improve the quality of life for those affected by this condition.

In addition to the updates on management recommendations, the second edition also includes new sections on topics such as the growth and development monitoring in children with SCD, educational and psychological counseling, transition of care for adolescents and young adults, Nutrition, and the role of support groups in SCD.

I would like to thank all the contributors to this second edition for their dedication and hard work in bringing this important resource to fruition. I hope that these guidelines will continue to serve as a valuable tool for healthcare professionals in the care of patients with SCD, and ultimately lead to improved outcomes for those living with this challenging disease.



Prof. Tumaini J. Nagu  
**CHIEF MEDICAL OFFICER**

## ACKNOWLEDGEMENT

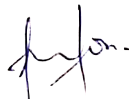
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The development of the Sickle Cell Disease Management Guidelines, 2nd edition, was a collaborative effort that involved the contributions of many individuals and organizations. The Ministry of Health (MoH) would like to express its heartfelt gratitude to all those who generously gave their time, expertise, and resources to make this project a reality.

First and foremost, MoH would like to thank patients, families, and caregivers who provided input and feedback on the guidelines during their development. Their perspectives were invaluable in shaping the guidelines and ensuring that they are relevant and useful for those affected by SCD. In this category we are very thankful to SCD Patients Community of Tanzania (SPCT) and Tanzania SCD Warriors (TASIWA)

We would like to thank the many organizations and institutions that supported the development of the guidelines, including the SCD program of MUHAS, Tanzania SCD alliance (TANSDA), Tanzania NCD Alliance (TANCDA), Muhimbili National Hospital (MNH) and Sickle Cell Youth Foundation (SCYF) who deserves recognition for their invaluable contributions in ensuring that the guidelines were developed with the highest standards of scientific rigor and clinical relevance. The MoH would also like to extend special thanks to Professor Paschal Ruggajo Director of Curative Services at the MoH, Dr Omary Ubuguyu, Assistant Director of NCD at the MoH, Dr Asteria Mpoti SCD coordinator at MoH, Asha Gembe, Shadrack Buswelu, Dr Erasmus Mndeme, and Dr Deogratias Soka, the Executive Director of TANSDA for their tireless efforts in ensuring the process of developing these guidelines is completed.

MoH would like to recognize the following authors and reviewers who contributed their knowledge and expertise to the guidelines; Dr Adam Kilungu, Dr Yonaz Mbenea, Dr Lulu Chirande, Dr Mwashungi Ali, Mr Yusuph Gesase, Dr Rachel Nungu and Dr Godbless Mfuru, for their dedication and attention to details, were critical to ensuring that the guidelines reflect the most current evidence-based practices in SCD care.



Prof. Paschal J. Ruggajo  
**DIRECTOR OF CURATIVE SERVICES**

## CONTENTS

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|                       |      |
|-----------------------|------|
| FOREWORD .....        | ii   |
| ACKNOWLEDGEMENT ..... | iii  |
| CONTENTS .....        | iv   |
| ABBREVIATIONS .....   | vii  |
| INTRODUCTION .....    | viii |

### **PART I: EMERGENCY MANAGEMENT ..... 1**

|                                                                                     |   |
|-------------------------------------------------------------------------------------|---|
| 1. IMMEDIATELY START EMERGENCY ASSESSMENT<br>AND TREATMENT .....                    | 1 |
| 1.1 Pain Relief .....                                                               | 2 |
| 1.2 Fluid Bolus (HYDRATION) .....                                                   | 2 |
| 1.3 Blood Transfusion within 30-60 minutes .....                                    | 2 |
| 1.4 Secondary Survey (HEENT and Systematic Assessment)<br>within 5-20 minutes ..... | 3 |
| 1.5 Blood Culture and IV Antibiotics .....                                          | 3 |
| 1.6 Imaging and Radiological Investigations .....                                   | 3 |
| 1.7 Documentation and Reassessment .....                                            | 4 |
| 1.8 Consultation and Disposition .....                                              | 4 |
| 2. PAIN RELIEF .....                                                                | 4 |
| 2.1 - General pain relief .....                                                     | 4 |
| 2.2 Morphine for severe pain relief .....                                           | 5 |
| 2.3 Treatment of morphine overdose .....                                            | 7 |
| 3. HYDRATION .....                                                                  | 7 |

### **PART II: MANAGING ACUTE COMPLICATIONS OF SCD ..... 9**

|                                                               |    |
|---------------------------------------------------------------|----|
| 1. Painful crisis .....                                       | 9  |
| 1.1 Painful Crisis: Limbs/Joints .....                        | 9  |
| 1.2 Abdominal Crisis AND Girdle Syndrome .....                | 10 |
| 2. FEBRILE ILLNESS .....                                      | 11 |
| 3. ACUTE CHEST SYNDROME (ACS) .....                           | 12 |
| 4. ACUTE SEVERE ANAEMIA .....                                 | 14 |
| 5. ACUTE SPLENIC SEQUESTRATION .....                          | 15 |
| 6. HEPATOBILIARY COMPLICATIONS .....                          | 16 |
| 6.1 Cholelithiasis (Gallstones) and acute cholecystitis ..... | 16 |
| 6.2 Intrahepatic Cholestasis .....                            | 16 |
| 7. NEUROLOGICAL COMPLICATIONS .....                           | 17 |

|                                      |    |
|--------------------------------------|----|
| 7.1 Stroke.....                      | 17 |
| 7.2 Seizures/Convulsions.....        | 18 |
| 8. GENITOURINARY COMPLICATIONS ..... | 20 |

### **PART III: MANAGING CHRONIC COMPLICATIONS OF SCD .....22**

|                                             |    |
|---------------------------------------------|----|
| 1. CHRONIC PAIN .....                       | 22 |
| 2. HYPERSPLENISM.....                       | 22 |
| 3. ORTHOPAEDIC COMPLICATIONS.....           | 23 |
| 3.1 Avascular Necrosis (AVN).....           | 23 |
| 3.2 Osteomyelitis and Septic Arthritis..... | 24 |
| 4. CHRONIC LEG ULCERS .....                 | 25 |
| 5. RENAL COMPLICATIONS .....                | 25 |
| 6. OPHTHALMOLOGIC COMPLICATIONS.....        | 26 |

### **PART IV: PREVENTIVE STRATEGIES AND HEALTH MAINTENANCE IN PATIENTS WITH SCD .....28**

|                                                            |    |
|------------------------------------------------------------|----|
| 1. PREVENTION OF INVASIVE INFECTION .....                  | 28 |
| 2. FOLATE SUPPLEMENTATION .....                            | 28 |
| 3. HYDROXYUREA THERAPY .....                               | 29 |
| 4. NUTRITION.....                                          | 31 |
| 5. GROWTH AND DEVELOPMENT MONITORING IN CHILDREN.....      | 32 |
| 6. EDUCATION AND PSYCHOSOCIAL COUNSELING .....             | 32 |
| 7. TRANSITION OF ADOLESCENTS TO ADULT CARE .....           | 33 |
| 8. TRAVEL MANAGEMENT .....                                 | 33 |
| 9. ORGANIZING SUPPORT GROUP .....                          | 34 |
| 10. REPRODUCTIVE HEALTH .....                              | 34 |
| 10.1 Reproductive Counseling.....                          | 34 |
| 10.2 Pregnancy in SCD.....                                 | 35 |
| 11. EARLY DIAGNOSIS THROUGH NEWBORN SCREENING (NBS) .....  | 36 |
| 12. PERI-OPERATIVE CARE IN SCD.....                        | 37 |
| 13. SCREENING FOR SPECIFIC CONDITIONS.....                 | 38 |
| 13.1 Screening for Renal disease .....                     | 38 |
| 13.2 Screening for Cardiovascular Diseases .....           | 38 |
| 13.3 Screening for Pulmonary Hypertension .....            | 38 |
| 13.4 Screening for Retinopathy .....                       | 39 |
| 13.5 Screening for risk of stroke using Neuroimaging ..... | 39 |

**PART V: OUTPATIENT MANAGEMENT OF SCD.....40**

1. THE NEW PATIENT APPOINTMENT ..... 41

2. THE FOLLOW-UP CLINIC ..... 42

3. TREATMENT PRESCRIBED IN CLINIC VISITS..... 44

4. LABORATORY DIAGNOSIS IN SCD ..... 44

**PART VI: BLOOD TRANSFUSION IN THE MANAGEMENT  
OF SICKLE CELL DISEASE..... 46**

1. ACUTE SIMPLE TRANSFUSION ..... 46

2. CHRONIC TOP UP TRANSFUSION ..... 46

3. EXCHANGE TRANSFUSION ..... 47

4. COMPLICATIONS OF BLOOD TRANSFUSION ..... 51

**REFERENCES ..... 52**

## **ABBREVIATIONS**

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|        |                                                    |
|--------|----------------------------------------------------|
| MAT    | Medical Association of Tanzania                    |
| MNH    | Muhimbili National Hospital                        |
| MoH    | Ministry of Health                                 |
| MUHAS  | Muhimbili University of Health and Allied Sciences |
| PAT    | Pediatric Association of Tanzania                  |
| SCD    | Sickle Cell Disease                                |
| SCP    | Sickle Cell Program                                |
| SCPCT  | Sickle Cell Patients Community of Tanzania         |
| SCYF   | Sickle Cell Youth Foundation                       |
| TANCDA | Tanzania Non-Communicable Disease Alliance         |
| TSDA   | Tanzania Sickle Cell Disease Alliance              |
| WHO    | World Health Organization.                         |

## INTRODUCTION

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This first edition Sickle cell disease (SCD) clinical management guideline is organized into six main parts: Emergency management of acute SCD complications, Management of chronic SCD complications, Preventive Strategies and Health Maintenance in Patients with SCD, Outpatient management of SCD and Blood transfusion in SCD. The sub topic of SCD diagnosis is contained in part five (Outpatient management of SCD)

This arrangement is made sequentially to ease and maintain the quality of management of the practice in health facilities all the way from primary; secondary and tertiary levels. The SCD clinical management guideline is intended to be used to equip knowledge to all health care providers dealing with management of SCD patients.

## PART I: EMERGENCY MANAGEMENT

Commonly, patients with sickle cell disease present to emergency unit or facilities with emergency conditions such as painful crisis, acute severe anaemia, respiratory distress, and loss of consciousness which requires emergency treatment.

When such patient presents to health facility do the following;

### 1. IMMEDIATELY START EMERGENCY ASSESSMENT AND TREATMENT

PRIMARY SURVEY (ABCDE) and VITAL SIGNS within 5 MINUTES of arrival

#### A Airway management

Assess and manage airway (clearing of secretions or foreign body, if any)

#### B. Breathing management

Assess for signs of compromised breathing (fast breathing (check respiratory rate), shortness of breath, decreased air entry bilaterally, hypoxia- check saturation of oxygen-SpO<sub>2</sub>-added sounds on chest auscultation)

If any signs of hypoxia (SaO<sub>2</sub> <90%), give oxygen, aim to maintain SpO<sub>2</sub> >95%)

#### C. Circulation management:-

Assess and document signs of shock (hypotension-check blood pressure), rapid weak pulse-check for pulse and heart rate, cold clammy extremities and poor capillary refill).

Start IV access then draw blood for full blood count, reticulocytes, liver function tests, urea, electrolytes, malaria test and grouping and cross-matching.

Check for Random Blood Sugar (RBG) if less than 2.5mmol/l, then start 10% Dextrose at 5mls/kg.

#### D. Disability management:

Assess level of consciousness (use AVPU or Glasgow Coma Scale (GCS) and neurological function assessment

## **E: Exposure:**

Expose and assess the patient (check the Temperature; if above 38.5 C provide antipyretic- Paracetamol 15mg/kg stat).

Take a quick history with particular attention to;

Allergy, Medication, Past medical history, Last meal, Events of current illness - AMPLE

**Allergy:** Inquire if the patient has any allergy to medication

**Medication history:** Inquire about the medication history of the patient

**Past medical history:** Inquire about the relevant past medical history of the patient,

**Last meal:** Inquire about the timing of last meal taken by the patient,

**Events leading to current illness:** Inquire about the history of the current illness

### **1.1 Pain Relief**

Give initial dose within 10 MINUTES of arrival at hospital

Give Paracetamol 15mg/kg PO +/- either Ibuprofen 10mg/kg PO or Diclofenac 1mg/kg PO 8 hourly

Or

Morphine 0.1 mg/kg IV 6 hourly (not exceeding 15 mg per dose)

Or

Morphine 0.2-0.5mg/kg PO 4hry (not exceeding 20mg/kg per dose)

Or

Pethidine 1mg/kg IV 6 hourly (not exceeding 100 mg per dose)

**NB: Assess pain and response to medication after 60 minutes, and provide subsequent doses as appropriate.**

### **1.2 Fluid Bolus (HYDRATION)**

***Within 10 MINUTES of arrival at hospital;***

Initiate fluid bolus to hydrate the patient (document intake and output)

Give orally if drinking well, give IV if poor oral intake or NIL by mouth

Initial IV fluid bolus (RL, NS, DNS ) should be 20mls/kg and may be repeated up-to three times (NB: Check and adjust the dose according to the level of pallor or hemoglobin)

### **1.3 Blood Transfusion within 30-60 minutes**

Anticipate the need for transfusion in patients with acute severe anemia, stroke, acute chest syndrome, girdle syndrome, or acute splenic sequestration.

Transfuse 10-15 mls/kg of blood (PRBCs) or 20mls/kg of whole blood within 30-60 minutes of hospital arrival or refer to appropriate facility with capacity to transfuse.

#### **1.4 Secondary Survey** (HEENT and Systematic Assessment) within 5-20 minutes

##### ***Perform Head to toe examination of the patient:***

HEENT- (Head, Eyes, Ears, Nose and Throat) assessment and management

CNS- (Central Nervous System) assessment and management

RS- (Respiratory System) assessment and management

CVS- (Cardiovascular System) assessment and management

GIT-Gastrointestinal System assessment and management

GU- Genital Urinary System assessment and management

MSS-(Musculoskeletal system) assessment and management

#### **1.5 Blood Culture and IV Antibiotics**

##### ***Within 60 minutes of arrival;***

In a patient with fever or respiratory distress, draw blood for culture and sensitivity and then initiate broad-spectrum antibiotics such as ceftriaxone and amoxicillin-clavulanic acid

***NB: Blood culture results should NOT delay the initiation of broad-spectrum antibiotics***

#### **1.6 Imaging and Radiological Investigations**

##### ***Within 60-120 minutes of arrival;***

In a patient with signs of respiratory distress do chest X-ray

In a patient with signs of skeletal disease do appropriate skeletal X-Ray

In a patient with signs of altered mental status or any neurological deficit do CT-Brain or transfer to a facility with such capacity.

In a patient with deep jaundice and tender hepatomegaly, do abdominal USS

## 1.7 Documentation and Reassessment

Within 120 minutes of arrival,

Document all the history, physical findings, initial management and interventions provided.

Reassess the patient's clinical condition (including vital signs, neurological status and relief of symptoms)

## 1.8 Consultation and Disposition

Consult the admitting team for all admitted patients to ensure continuity of care.

All discharged patient must have follow-up appointment within one week

## 2. PAIN RELIEF

All patients must receive analgesia within 10 minutes of admission, according to the severity of their pain. Reassess after 1 hour and give further analgesia if needed.

Provide adequate pain medication and taper down as pain decreases and the patient improves.

Ensure pain medications are given regularly (do not wait for the pain to recur)

### 2.1 - General pain relief

| Severity | Management                                                                                                                                                                          |
|----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mild     | Reassurance, hot packs, reposition, massage, distraction (stories, play)<br>Child: Paracetamol 15mg/kg PO 6hourly<br>Adult: Paracetamol 1g PO 6hourly                               |
| Moderate | As for mild pain, PLUS<br>Child: Ibuprofen 10mg/kg PO 8 hourly OR Diclofenac 1mg/kg PO 8hourly<br>Adult: Ibuprofen 400mg PO 8 hourly OR Diclofenac 100mg PO 8hourly                 |
| Severe   | As for moderate pain PLUS<br>Child: Morphine 0.2-0.5mg/kg PO 4 hourly (not exceeding 20mg/kg/dose)<br>Infants: Morphine 0.1mg/kg PO 4 hourly<br>Adult: Morphine 10-20mg PO 4 hourly |

## 2.2 Morphine for severe pain relief

Oral morphine is the drug of choice for children with severe pain. Children can tolerate very large doses of morphine if titrated appropriately. The dose must be adjusted for each child.

Start Initial Dose based on the patient's age and weight

1-12 months      0.1mg/kg PO    4 hourly

1-12 years        0.2-0.5mg/kg    4 hourly

Give this dose regularly every 4 hours.

Prescribe the same dose for 'breakthrough pain' to be repeated as often as necessary between regular doses in PRN.

Review after 24-48 hours and adjust the scheduled dose according to the amount of breakthrough medication that the patient has used in the past 24 hours.

Increase the Dose based on patient's use of breakthrough medication  
If needed, add 20%-30% of the previous dose (e.g. from 1 mg to 1.2mg).

Minimum increase 20%, maximum increased 50%.

***Give Laxative for all patients using morphine for more than 24 hrs to prevent constipation***

Forms available:

Oral: immediate release liquid morphine, 10mg/5mL (more concentrated solution is also available)

Side Effects: These are to be expected and so do not usually necessitate dose change

|                     |                                    |                                                                                                                |
|---------------------|------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Nausea/<br>Vomiting | Usually wears off in<br>24-48 hrs. | Warn and reassure patients/parents.<br>Use antiemetic (metoclopramide or<br>domperidone).                      |
| Pruritus            | Usually wears off in<br>3-4 days   | Use antihistamines.<br>Exclude infectious causes or reaction to<br>antibiotics.                                |
| Drowsiness          | Usually reversed in<br>2-3 days    |                                                                                                                |
| Constipation        | Common                             | Always prescribe laxatives e.g.<br>lactulose when starting opioids.<br>Titrate laxative dose with opioid dose. |

### Alternatives to Oral Route:

The oral route is the route of choice and should be used whenever possible. Occasionally an alternative route may be required – intravenous or subcutaneous.

### Conversion from PO to IV

Divide oral dose in half to obtain an equal -analgesic dose. For example, if the patient is receiving 2mg 4hrly PO, the proper dose for IV would be 1mg 4hrly IV.

### Initial Morphine Loading Dose IV:

0.05–0.1mg/kg over 10 minutes.

Patient must be pain free by bolus morphine before commencing infusion.

### Continuous Infusion Rates:

|                      |                                                                          |
|----------------------|--------------------------------------------------------------------------|
| 0 – 3 months:        | Average initial rate 10microgram/kg/hr.<br>Range 5 – 15 microgram/kg/hr  |
| 3 – 6 months:        | Average initial rate 15 microgram/kg/hr<br>Range 5 – 20 microgram/kg/hr  |
| 6 months – 18 years: | Average initial rate 25 microgram/kg/hr<br>Range 10 – 40 microgram/kg/hr |

### **Preparation of infusion of morphine:**

Weight (kg) = Mg morphine (e.g. 10kg child draw up 10mg of morphine)

Mix in 5% dextrose to a total volume of 50ml

This gives a concentration such that an infusion rate of 1ml/hr = 20microgram/kg/hr.

Max concentration 50mg/50ml.

If pain is not responding to increased analgesia then check

Is dose appropriate? (check weight)

Is route appropriate? (e.g. vomiting child may not be absorbing)

Have you maximized co-analgesics?

Is pain opioid sensitive? (some pain e.g. neuropathic pain does not always respond fully to opioids)

Would anaesthetic procedure e.g. nerve block be helpful?

Would palliative radiotherapy help? e.g. bone pain.

Remember psychosocial issues (e.g. fear, anxiety or low mood may contribute to pain experience).

## 2.3 Treatment of morphine overdose

Naloxone, an opioid antagonist, is the antidote to morphine. It is used for the reversal of life-threatening opioid-induced respiratory depression. It should NOT be used for drowsiness and/or delirium which is not life threatening because of the danger of totally reversing the opioid analgesia and precipitating severe/agonizing pain.

Initial Dose:

10 microgram/kg (Max 8mg) IV

Repeat Doses:

100microgram/kg (Max 2mg) IV as a single dose

Repeat as necessary to maintain opioid reversal.

## 3. HYDRATION

Patients with SCD are at risk of dehydration due to impaired renal concentrating power and poor fluid intake.

Encourage oral fluids first, it should be used whenever possible

Give IV fluids if the patient is unable to drink well or has severe pain.

Use fluids such as RL, NS and DNS.

Stop IV fluids when the patient is stable and pain is controlled

Maintain a strict input/output chart for every patient

For children, weigh them daily

Fluid Calculations: Give maintenance fluid x 1.5

| Body weight (kg)                                                      | Fluids (ml/kg/day)                                                                 |
|-----------------------------------------------------------------------|------------------------------------------------------------------------------------|
| <10 kg                                                                | 150ml/kg/day                                                                       |
| 11 – 20kg                                                             | 1500ml for the first 10kg of weight plus 75ml/kg/day for every kilogram above 10kg |
| > 20kg                                                                | 2250ml for the first 20kg of weight plus 30ml/kg for every kilogram above 20kg     |
| Divide the total daily volume by 24 hours to obtain hourly fluid rate |                                                                                    |

**CAUTION!**

In stroke, there is a risk of cerebral edema, therefore, watch out for fluid overload

In acute chest syndrome, there is a risk of pulmonary edema, watch out for fluid overload.

In these patients, initially give half of the volumes in the table. Reassess hydration status regularly, modify fluids accordingly.

## PART II: MANAGING ACUTE COMPLICATIONS OF SCD

A full systemic examination is required for all individuals in order to establish diagnosis and rule out presence of other complications.

Full Blood Picture should be done for all individuals presenting to a health facility with acute complications of SCD.

Additional investigations will depend on the specific complication present and are listed in the respective sections.

### 1. PAINFUL CRISIS

**Pain is usually due to an acute vaso-occlusive crisis. Always prescribe regular analgesia – not ‘PRN’**

- **Symptoms/signs:**
- Assess degree of pain: Use pain assessment tool. Ask the patient to rate pain as mild, moderate or severe. If the patient is a very young child, accept the parent’s assessment.
- **Ask about history of pain:** Site, severity and duration of pain (usually long bones, spine and abdomen). Any dactylitis/hand-foot syndrome (commonly in infants).
- **Ask about medications:** What did they take so far for this crisis, what medications have worked previously (Refer to SCD health passport if present)
- Full systemic examination to look for complications

#### 1.1 Painful Crisis: Limbs/Joints

**Most commonly, limb pain is caused by vaso-occlusive crisis, but differentials include; septic arthritis, osteomyelitis or avascular necrosis.**

##### **Investigations:**

- Full blood count
- If febrile do blood culture, malaria test, and inflammatory markers such as C - reactive protein (CRP) and ESR. If fever does not respond to antibiotics after 48 hours, consider bone ultrasound or x-ray (x ray changes of acute osteomyelitis take 10-14 days to appear, therefore a normal x ray does not rule out acute osteomyelitis)
- If suspicious for septic arthritis, consider arthrocentesis

### **Management:**

- GIVE ANALGESIA as per pain guideline on page 6
- Insert IV cannula and collect blood for investigations.
- IF FEBRILE, commence antibiotics.
- If clinically suspected osteomyelitis/septic arthritis refer to page 28 on management of osteomyelitis or consult surgeons/orthopedic surgeon

## **1.2 Abdominal Crisis AND Girdle Syndrome**

**Abdominal vaso-occlusive crisis:** Abdominal distension with generalized abdominal tenderness (but no rebound tenderness) and reduced bowel sounds. Abdomen moves with respiration, vomiting and diarrhea are not common.

**Girdle (mesenteric) syndrome:** established ileus with vomiting, constipation, silent distended abdomen, distended bowel loops and fluid levels on abdominal X-ray. High risk of developing acute chest syndrome.

### **Differential diagnosis:**

- Hepatitis
- Peptic ulcer
- Surgical: Acute appendicitis; Cholecystitis; Acute pancreatitis; Biliary colic

### **Investigations:**

- Full blood count
- Group and cross-match if transfusion likely
- Creatinine, urea, electrolytes, ALT, bilirubin total and direct.
- If febrile, blood cultures ,urine cultures and malaria test
- Abdominal x-ray and chest x-ray within 4 hours of admission
- Abdominal ultrasound if worsening jaundice

### **Management:**

- **GIVE ANALGESIA** as per pain guideline
- Place IV cannula and collect blood for investigations.
- **IV FLUIDS** – hyper hydrate, as per hydration guideline
- **IF FEBRILE**, commence antibiotics
- Nil by mouth if vomiting, abdominal distension or absent bowel sounds

- Insert NG tube and place on free drainage if vomiting
- Laxatives if constipation and no ileus (bowel sounds present)
- Request surgical review if acute abdomen
- HOURLY OBSERVATIONS – pulse, respiratory rate, oxygen saturations
- MEASURE ABDOMINAL GIRTH 1 to 4 hourly – monitor for distension and spleen size

## 2. FEBRILE ILLNESS

**Patients with SCD are at risk of overwhelming septicemia with encapsulated organisms, due to loss of normal splenic function.**

### **Symptoms and signs:**

- Symptoms and signs reflect the underlying illness e.g. fever, runny nose, tachycardia, tachypnea, enlarged hyperemic tonsils, convulsions etc.

### **Possible Causes Include:**

- Local viral or bacterial infections: rhinitis, pharyngitis, tonsillitis, otitis media, etc.
- Painful crisis: vaso-occlusive crisis can cause a low-grade fever, but temperature is above 38.5 degrees in only 5% of patients in the absence of infection.
- Generalized viral illness: measles, chicken pox etc.
- Malaria
- Severe systemic infection e.g. septicemia, pneumonia, meningitis, osteomyelitis, UTI etc.
- Acute chest syndrome – always suspect if fast breathing or SPO2 < 95% (or 2% below the steady state).

### **Investigations:**

- **Full blood count, blood culture and sensitivity, CRP and malaria test**
- **Urinalysis (dipstick), urine microscopy, and urine culture and sensitivity**
- Blood grouping, cross-match and save, creatinine, electrolytes.
- Chest x-ray if any respiratory symptoms and signs
- Bone imaging +/- orthopedic review when clinically suspicious of septic arthritis or acute osteomyelitis.
- Lumbar puncture when clinically suspicious of meningitis.

**Indications for inpatient care.**

Temperature >40 degrees Celsius, or temperature 38 - 40 degrees Celsius with any one of the following

- Tachycardic, tachypneic, poorly perfused, drowsy or hypotensive.
- Severe painful crisis
- Acute changes in spleen size reported by parent
- Infiltrates on chest X-ray
- Hb <5g/dl or acute drop in Hb > 2g/dl from steady state hemoglobin value.
- Symptoms indicative of stroke or neurological deficit.

**Management:**

- Insert IV cannula and collect blood for investigations.
- Give antipyretics-to lower the temperature
- Give broad spectrum antibiotics such as IV ceftriaxone 70-100mg/kg once daily or amoxicillin clavulanic acid 30mg/kg/dose 8hourly for 10 days.
- Consider: malaria treatment, oxygen, pain relief, transfusion if indicated
- IV fluids – Hydrate, as per hydration section page.
- Hourly observations for first 6-12 hours – pulse, respiratory rate, SPO<sub>2</sub>, temperature, GCS – be alert for complications e.g. chest syndrome, stroke.

**Prevention planning (prior to discharge):**

- Immunizations
- Prophylactic penicillin V
- Insecticide treated net
- Education and counseling on hygiene, safe drinking water, prevention of infection, when to seek medical care

**3. ACUTE CHEST SYNDROME (ACS)**

**Any patient with SCD has the potential to develop a chest crisis, no matter how they first present.**

**Symptoms and signs:**

**Treat as chest crisis if presents with** signs and symptoms of respiratory distress (fast breathing, chest wall recession, nasal flaring, grunting, and hypoxia – SPO<sub>2</sub> <95% on air) and /or any of the following:

- Pain – often pleuritic (worse with breathing), in the chest wall, abdomen or back.

- Cough
- Wheeze
- High fever, tachycardia
- Infiltrates on chest x ray

### **Investigations:**

- Arterial blood gases, creatinine, electrolytes, ALT
- Full blood count, malaria test, blood and urine culture and sensitivity, CRP
- Chest X-ray – physical signs often precede chest X-ray changes
- HPLC (to establish baseline Hemoglobin S percent for possible exchange transfusion).

### **Management:**

- Pain relief – as per pain protocol on page 11, caution not to over-sedate with opioids
- Place an intravenous cannula and collect blood for investigations.
- Oxygen - Give supplemental oxygen to maintain oxygen saturation of greater than 95 percent
- Fluids – hydrate as per hydration protocol on page 15, but caution not to fluid overload – reassess regularly.
- Give broad spectrum antibiotics such as IV ceftriaxone 70-100mg/kg once daily or amoxicillin clavulanic acid 30mg/kg/dose 8hourly for 10 days.
- Give Macrolides such as Azithromycin or Clarithromycin to cover for atypical microorganisms.
- Top up blood transfusion - Give 10 mLs/kg PRBCs to people with symptomatic ACS whose hemoglobin concentration is >1.0 g/dL below baseline. If baseline hemoglobin is 9 g/dL or higher, top up blood transfusion may not be required.
- Exchange blood transfusion - Perform urgent exchange transfusion when there is rapid progression of ACS as manifested by oxygen saturation below 90 percent despite supplemental oxygen, increasing respiratory distress, progressive pulmonary infiltrates, and/or decline in hemoglobin concentration despite simple transfusion.
- Maximum time from decision to starting transfusion = 12 hours
- Incentive spirometry (example blowing a balloon)
- Mobilize as soon as possible
- Inform anesthetist/intensivist early – mechanical ventilation may later be required

- Continuous hourly monitoring – pulse, respiratory rate, oxygen saturations by pulse oximetry

**Note: This is life threatening - admit in a high dependency unit or intensive care unit (ICU)**

#### **4. ACUTE SEVERE ANAEMIA**

Defined as hemoglobin <5g/dl or recent acute drop in Hb  $\geq$ 2g/dl below steady state or acutely symptomatic anemia (tachycardia, tachypnea, tender hepatomegaly)

##### **Possible causes:**

Infection e.g. malaria, bacterial infection

Splenic sequestration

Hemolysis (jaundice, inter current illness/ infection, high reticulocyte count)

Aplastic crisis due to Parvovirus B19 (low reticulocyte count)

Bleeding

##### **Investigations:**

- Immediately blood grouping and cross-match 10-15ml/kg packed red cells
- Full blood count, reticulocyte count , creatinine, electrolytes, haptoglobin, bilirubin, LDH and ALT
- Urine microscopy for RBC and dipstick for urobilinogen
- Blood and urine cultures if febrile or signs of infections
- Malaria test

##### **Note:**

***In hemolysis expect high reticulocyte count, unconjugated bilirubin, LDH,urine urobilinogen and low haptoglobin***

***In aplastic crisis expect low reticulocyte count, normal bilirubin and LDH***

##### **Management:**

- Place an intravenous cannula and collect blood for investigations.
- Immediately transfuse Packed RBC 10-15mls/kg over 4hours if symptomatic or Hb <5g/dl
- Treat the underlying cause where applicable
- Blood transfusion may be repeated if control Hb is <5g/dl or the patient is still symptomatic.
- Assess and document size of liver and spleen

## 5. ACUTE SPLENIC SEQUESTRATION

Splenic sequestration is characterized by sudden enlargement of the spleen due to trapping of significant proportion of blood volume, rapid drop in hemoglobin, hematocrit, hypovolemia and thrombocytopenia. It is most common in infants and children and tends to be recurrent. Hepatic sequestration can also occur, usually in children > 4 years old.

### **Symptoms and signs**

- Pallor, lethargy, hypotension, tachycardia, hypovolemia shock
- Abdominal pain /tenderness
- Abdominal distension with tender splenomegaly

### **Investigations:**

- Blood grouping and cross-match

Full blood count, reticulocyte count, electrolytes, creatinine, ALT, LDH; consider blood cultures, malaria test

### **Management:**

- Place an intravenous cannula and take blood for investigations
- Immediately give 20 ml/kg Normal saline bolus whilst awaiting blood, repeat bolus if needed
- Transfuse 5-7.5mls/kg (50% of what we would commonly transfuse) over 3-4 hours
- Give oxygen if needed.
- Give analgesics if needed
- Check Hb 2 hours post-transfusion consider repeat transfusion
- Monitor SPO<sub>2</sub>, respiratory rate, pulse rate and blood pressure at least every 30 minutes.
- Monitor spleen size hourly for 12-24 hours until reducing in size
- Therapeutic splenectomy is indicated if >2 episodes of sequestration

### **Note**

***This is life threatening condition, may need high dependency care  
There is high risk of developing acute chest syndrome.***

## 6. HEPATOBIILIARY COMPLICATIONS

### 6.1 Cholelithiasis (Gallstones) and acute cholecystitis

Patients with SCD have a high incidence of pigment gallstones due to chronic haemolysis. Gallstones are usually asymptomatic, however may cause inflammation of the gallbladder wall (Cholecystitis).

#### **Symptoms and signs**

Abdominal pain (commonly right upper quadrant)

Deepening of Jaundice

#### **Differential diagnosis:**

- Abdominal vaso-occlusive crisis and Girdle syndrome
- Acute and chronic cholecystitis
- Acute pancreatitis, Hepatitis, Peptic ulcer
- Hepatic sequestration
- Acute chest syndrome

#### **Investigations:**

- Bilirubin total and direct, ALT, ALP, AST, LDH, GGT, albumin
- Full blood count
- PT/PTT
- Abdominal ultrasound
- Plain abdominal x-ray (approx. 50% of stones are radio-opaque)

#### **Management:**

- Give analgesia if in pain
- Give iv fluids, hydrate as per hydration guideline
- Give antibiotics if clinically suspicious of infection (febrile): Amoxicillin clavulanic acid or Amoxicillin in combination with Metronidazole and Gentamicin (if the patient is very sick give parenterally)

#### ***Note***

***Recurrent episodes of cholecystitis are an indication for cholecystectomy. Refer for surgical opinion regarding elective cholecystectomy.***

### 6.2 Intrahepatic Cholestasis

Intrahepatic cholestasis is characterized by severe hyper-bilirubinemia (conjugated and unconjugated) and moderately raised alkaline phosphatase (ALP), associated with fever and hepatic pain in the absence of demonstrable stones. These episodes are thought to be due to severe intra-hepatic sickling.

## **Symptoms and signs**

Abdominal pain (commonly right upper quadrant)

Deepening of Jaundice

Fever

## **Investigations**

- Bilirubin total and direct, ALT, ALP, AST, LDH, GGT, albumin
- Full blood count, PT/PTT
- Abdominal ultrasound

## **Management:**

- Give analgesia if in pain
- Give iv fluids, hydrate as per hydration guideline
- Give antibiotics if clinically suspicious of infection (febrile): Amoxicillin clavulanic acid or Amoxicillin in combination with Metronidazole and Gentamicin (if the patient is very sick give parenterally)
- Monitor liver size and function
- Frequent blood transfusions may be needed in case of hyperhaemolysis or sequestration
- Exchange transfusion may be needed in severe cases

## **7. NEUROLOGICAL COMPLICATIONS**

### **7.1 Stroke**

Stroke is a common and potentially devastating manifestation of SCD that can affect children and adults. Previous stroke and high trans-cranial Doppler ultrasound (TCD) velocities ( $>200\text{cm/sec}$ ) are the major risk factors.

## **Signs and symptoms:**

- Slurred speech, blurred vision, limp, weakness of one or more limbs
- Abnormal behavior, sudden personality change
- Severe headache
- Seizures, altered level of consciousness, coma

## **Investigations:**

- Random blood glucose, brain CT scan
- Full blood count, HPLC, electrolytes, creatinine, ALT, LDH
- Blood and urine cultures, malaria test if clinically indicated
- Consider lumbar puncture if infection or subarachnoid hemorrhage possible
- TCD and MRA (magnetic resonant brain angiography)

**Management:**

- Ensure airway patency and give oxygen if indicated
- Place an intravenous cannula and take blood for investigations
- Give 10% glucose if hypoglycemic
- If convulsing give diazepam 0.5mg/kg rectally or 0.15-0.3mg/kg IV (if convulsions persists for more than 10 minutes repeat same dose of diazepam). If convulsions persist give loading dose of phenobarbitone 20mg/kg IV/IM.
- Give IV fluids cautiously at 60% of maintenance due to risk of cerebral edema.
- Give antibiotics if suspicious of meningitis: IV ceftriaxone 100mg/kg once a day
- Give antimalarial if indicated
- Do exchange transfusion within 4 hours of admission (to achieve Hb S < 30%) if not possible give top up blood transfusion (Maintain Hb around 10g/dl).
- A second exchange transfusion can be considered depending on neurological status and Hb S level
- Give dexamethasone if evidence of raised intracranial pressure (if there is no cerebral hemorrhage)
- In case of cerebral hemorrhage consult neurosurgeons
- Hourly neurological observations (level of consciousness/power)
- Initiate Hydroxyurea ( ref to hydroxyurea chapter)
- Provide physiotherapy and occupational therapy

**7.2 Seizures/Convulsions**

Children with cerebrovascular disease, e.g. silent infarcts, are more prone to febrile seizure. Seizures are also common after stroke, subarachnoid hemorrhage or sagittal sinus thrombosis.

**Immediate action:**

- Follow the protocol for SCD emergency management pg9
- Give anticonvulsants, usually diazepam (slow IV injection or per rectal)
- Start antibiotics if the patient is febrile
- Give antipyretics (Paracetamol +/- Non steroidal anti-inflammatory drugs if febrile)

### **Investigations**

- RBG
- FBP, Urea, HPLC, electrolytes, ALT, Ca+, Mg, LDH, creatinine
- Blood and urine cultures, malaria test if clinically indicated
- lumbar puncture if clinically indicated (e.g. infections, subarachnoid hemorrhage)
- Imaging
  - Electroencephalogram (EEG)
  - CT Scan of Brain
  - MRI/MRA and diffusion scanning of Brain
  - Transcranial Doppler Studies (TCDs)

### **Management**

- Ensure airway patency and give oxygen if indicated
- Place an intravenous cannula and take blood for investigations
- Give 10% glucose if hypoglycemic
- Give diazepam 0.5mg/kg rectally or 0.15-0.3mg/kg IV (if convulsions persist for more than 10 minutes repeat the same dose of diazepam). If convulsions persist give loading dose of phenobarbitone 20mg/kg IV/IM.
- Give antibiotics if suspicious of meningitis: IV ceftriaxone 100mg/kg once a day
- Give antimalarial if indicated
- Limit rehydration to 60% maintenance
- In case of cerebral hemorrhage consult neurosurgeons
- Hourly neurological observations (level of consciousness/power)
- Initiate Hydroxyurea ( ref to hydroxyurea chapter 4)

### **Note:**

- If evidence of ischemia on MRI scanning, stenosis on MRA or abnormal TCDs, organize exchange transfusion.
- If the patient had fulfilled the International League Against Epilepsy (ILAE) definition for Epilepsy, treat accordingly (i.e. Carbamazepine for Focal Epilepsy and Sodium Valproate for Generalized Epilepsy).

## 8. GENITOURINARY COMPLICATIONS

### **Priapism**

A painful persistent penile erection that is unrelated to sexual stimulation. It can be acute/fulminant (lasting > 4 hours) or stuttering (repeated painful erections lasting more than 30 minutes and up to 4-6 hours). If priapism is untreated it can result into erectile dysfunction (ED) and impotence. Prolonged priapism is an emergency that requires urgent referral for urological assessment and intervention.

### **Investigations**

FBP, HPLC

### **Management**

- If episodes less than 2 hours from onset;
  - Give analgesia as per pain guideline
  - Document the time of onset and precipitating factors e.g. trauma, infection, use of drugs (e.g. alcohol, psychotropic agents, Sildenafil, Testosterone, Cocaine)
- Give anxiolytic agents for anxiety if indicated (e.g. lorazepam 0.05mg/kg/dose given 2-3 times per day, do not exceed 2mg/dose).
- Increase fluid intake orally or IV if indicated as per rehydration guideline
- Encourage patients to micturate, walk or have a warm bath.

For episodes lasting more than 2 hours,

- Keep the patient nil per oral in case of surgical intervention
- Continue IV hydration, analgesics and anxiolytics
- Catheterize if unable to micturate
- Grouping and cross match for possible exchange transfusion
- consult urologist/surgeon (for possible penile aspiration, intracorporeal injection of Phenylephrine  
**Or** wash out) **OR** refer to the next level facility with adequate expertise and facilities.

### **Procedure for intracorporeal injection of Phenylephrine:**

- Add 1 ml of 1% Phenylephrine (10mg/ml) to 39 ml of 0.9% saline to produce solution of 0.25mg/ ml
- Inject 0.25 mg Phenylephrine stat (i.e. 1 ml) directly into corpus cavernosum with 27-gauge needle

- Injection can be repeated every 15 minutes up to a maximum of 6 injections
- If no detumescence consider corpora spongiosum drainage

**Note:**

Complications of surgical treatment include bleeding, infections, skin necrosis, and damage to the structures of the urethra, fistulae and impotence.

Educate male patients with SCD about priapism and encourage them to inform their parents, guardians or doctors.

## PART III: MANAGING CHRONIC COMPLICATIONS OF SCD

### 1. CHRONIC PAIN

This is pain lasting for 3 or more months.

Chronic pain may occur with or without objective signs of avascular necrosis, arthropathy, arthritis, leg ulcers or vertebral body collapse.

#### Management

In addition to the pain management guideline on page 6;

- Investigate and manage the underlying cause of pain
- Encourage activities that offer pain relief, e.g. deep pressure massage, muscle relaxation therapy, yoga and hydrotherapy
- Consider management of neuropathic pain by antineuralgic (e.g. gabapentin or carbamazepine) or tricyclic antidepressants (e.g. amitriptyline)
- Use long (e.g. Morphine extended release capsules, tramadol) and short acting opioid to manage chronic pain that is not relieved by non-opioids.
- Patients with progressive musculoskeletal conditions should be referred to orthopedic or rheumatology specialist
- Refer for evaluation by psychologist to relieve anxiety / depression stemming from disability, job absence or financial difficulties
- Refer to occupational therapist and physiotherapist to assist patients to gain optimum physical function and independence.

### 2. HYPERSPLENISM

Hypersplenism is characterized by splenomegaly and cytopenia of at least two cell lines.

#### Symptoms and signs:

- Pallor, lethargy
- Abdominal distension with chronic splenomegaly
- Cytopenia

#### Investigations:

- FBP
- Reticulocyte count

- Peripheral smear
- Iron studies
- Bone marrow aspirate (in case of low reticulocyte count)
- PT/PT/INR (if splenectomy anticipated)

#### **Management:**

- Exclude and treat all causes of anemia
- Transfuse if Hb is below 4 g/dl
- Monitor spleen size and document at every visit
- Refer to surgical department for elective splenectomy

### **3. ORTHOPAEDIC COMPLICATIONS**

#### **3.1 Avascular Necrosis (AVN)**

It causes chronic pain and limitation of movement due to joint damage (rather than ongoing vaso-occlusion).

AVN commonly affects the femoral head (hip) or humeral head (shoulder). Adolescents are commonly affected but may start in early childhood.

#### **Symptoms and signs:**

- Severe pain and decreases mobility
- Pain with internal or external rotation of the joint
- Decreased ability to abduct the joint
- An antalgic gait (gait that favors weight bearing on the unaffected joint)

#### **Investigations:**

- Plain X-ray
- MRI (will show changes earlier than x-ray)

#### **Management:**

- Provide non-steroidal anti-inflammatory agents +/- codeine derivatives for acute pain
- Refer to management of chronic pain (part 3, page 27)
- Rest and avoid weight bearing of the affected joint (for at least 3 months)
- Non weight bearing physiotherapy - refer to physiotherapist
- Continue with hydroxyurea therapy
- Refer for orthopedic assessment and treatment

### **Notes on Orthopedic Surgical Interventions for AVN:**

- Hip replacement surgery is generally delayed until the mid-20s, because the replacement will only last for 10-20 years and then needs to be replaced.
- Tenotomy to improve range of movement or osteotomy and / or decompression surgery to improve joint prior to the end of adolescent growth phase.
- Joint replacement may become necessary if pain is continuous (> 2 years) or very severe, and if the patient's mobility is seriously affected
- Different types of prosthesis, hip fusion, or bone grafting are used depending on the individual case. Cemented prostheses are best avoided (to facilitate 're-do').
- Infection and loosening of the prosthesis are common
- The possibility of failure, the likelihood of some residual pain, the potential life of the prosthesis, and the limitations imposed must always be discussed with the patient pre-operatively
- Give blood transfusion prior to tenotomy or osteotomy and for 3 months post-operatively to maximize bone healing

### **3.2 Osteomyelitis and Septic Arthritis**

Bacterial infection of bones and joints are common in children and adults with SCD. Common organisms are *S. aureus*, *Salmonella* and *S. pneumoniae*.

#### **Symptoms/signs:**

- Vague bone pain
- Fever (may not be persistent)
- Inability to ambulate or limping
- Persistent signs of inflammation around the site (redness, tenderness, warmth, swelling)
- Draining sinus tracts (in chronic osteomyelitis)

#### **Investigations:**

- FBP
- Blood for culture and sensitivity
- CRP
- X-Ray: changes in osteomyelitis do not appear until at least 10 days after the onset.
- Ultra sound and MRI of affected bone

- Joint aspiration: is useful to identify organisms if fluid has been seen on ultrasound

**Management:**

- Give IV Ceftriaxone 100mg/kg OD or IV Amoxicillin clavulanic acid 30mg/kg 8 hourly for at least 10 days then continue with oral third generation cephalosporin such as Cefixime or oral Amoxicillin clavulanic to complete at least three weeks of treatment.
- Consult orthopedic surgeon

#### **4. CHRONIC LEG ULCERS**

Leg ulcers are frequent in late adolescence and adults with SCD especially males and patients with low steady state haemoglobin levels. Ulcers commonly arise near the medial or lateral malleolus, may be single or multiple and are painful and resistant to healing.

**Management:**

Treatment of ulcers requires multidisciplinary approach

Generally, treatment includes

Provide pain relief (including local pain control before wound dressing)

Reduce edema by resting the leg, elevation and compression bandage

Bed rest is important for healing of large and recalcitrant ulcers,

Debridement is important to remove necrotic tissue and stimulate healing

Regular wound cleaning and dressing

If there is local infection gives topical antibiotics

Some patients may benefit from chronic blood transfusion and skin grafting.

#### **5. RENAL COMPLICATIONS**

Renal involvement is common; up to 20% of patients with SCD develop renal insufficiency.

**Renal manifestations of SCD include:**

- Inability to concentrate urine with hyposthenuria
- Painless hematuria
- Microalbuminuria or proteinuria
- Hypertension
- Acute Kidney Injury (AKI)
- Chronic Kidney Disease and End-stage Renal Failure

**Investigations:**

- Urinalysis (dipstick and microscopy)
- 24-hour urine protein determination if proteinuria detected by urine dipstick
- Serum creatinine, urea and electrolytes (Potassium, Sodium, Calcium, Phosphorus)
- Estimate glomerular filtration rate (GFR)
- Serum electrolytes (hypernatremia, hyperkalemia)
- HIV, HBV and HCV (transfusion related infectious diseases)
- ECG and Echocardiogram if clinically indicated
- Renal ultrasonography - to exclude other causes of post renal or obstructive uropathy (nephrolithiasis)
- Cystoscopy, CT scan and renal biopsy if clinically indicated

**Management**

- Close monitoring of fluid intake and output should be performed
- Review by a nephrologist for a possible renal replacement therapy (e.g. hemodialysis, peritoneal dialysis, and renal transplantation) or refer to the next level facility with adequate expertise and facilities.
- Potential nephrotoxic drugs and imaging contrasts should be avoided

**6. OPHTHALMOLOGIC COMPLICATIONS**

- Sickle cell disease can cause retinopathy which is commonly observed in older children and adolescents and tend to progress throughout adulthood.
- Consider orbital cellulitis/orbital compression syndrome if a patient presents with proptosis, orbital swelling and pain, headache, impaired vision.
- Immediately examine for hyphema anyone with SCD who presents with eye trauma. If hyphema is present, immediately refer to an ophthalmologist for further management.
- These are relatively common and may occur in any vascular bed of the eye and may not be detected at their early stages unless an eye examination is performed annually
- Treatment may be medical or surgical and is aimed at preventing vision loss from vitreous hemorrhage, retinal detachment and epiretinal membranes

- In case of orbital cellulitis /orbital compression syndrome give analgesics, hydration and broad-spectrum antibiotics,
  - Promptly refer to an eye specialist anyone with SCD exhibiting signs and symptoms such as
- Protrusion of the eye
  - Changes in visual acuity
  - Unilateral or bilateral loss of vision

## PART IV: PREVENTIVE STRATEGIES AND HEALTH MAINTENANCE IN PATIENTS WITH SCD

### 1. PREVENTION OF INVASIVE INFECTION

#### ■ Phenoxymethyl Penicillin (Penicillin V)

Give Penicillin V to all children below 6 years of age

- 125 mg PO 12 hourly for children younger than 3 years
- 250 mg PO 12 hourly for children 3 years and older
- Children with SCD who have had surgical splenectomy should continue on penicillin prophylaxis indefinitely

#### ■ Immunization

Ensure that all infants with SCD receive all the scheduled vaccination according to the national Immune and Vaccine Development (IVD) programme which includes vaccine against pneumococcal pneumonia:

- Pneumococcal conjugate vaccine (PCV-13) – from 6 weeks of age, 3 doses 4 weeks apart (i.e. at age 6 weeks, 10 weeks and 14 weeks) and a booster dose between 12 - 15 months. If the child has not previously received this vaccine, then at least one dose should be given between 6 and 18 years.
- Pneumococcal polysaccharide vaccine (PPSV-23) - at 2 years then two boosters of 5 years apart
- Salmonella typhi Immunization should be given every 2 years if available.

#### **Note:**

Seek immediate medical attention whenever they are sick [fever, cough and Difficult In Breathing (DIB)] due to the risk of severe bacterial infections.

### 2. FOLATE SUPPLEMENTATION

- Patients with SCD needs folate supplementation due to high red blood cell turn over
  - Give Folic acid 5mg PO once daily for life

### 3. HYDROXYUREA THERAPY

Hydroxyurea is useful in the management of individuals with SCD. It reduces the complications of SCD in infants, children and adults based on its ability to:

- Increase haemoglobin F levels
- Increase steady state hemoglobin counts
- Lower WBC and PLTs hence moderate the chronic inflammation state in SCD

#### Indications for starting hydroxyurea:

- All from 9 months of age and all adults with SCD should receive hydroxyurea
- Once initiated, hydroxyurea should be continued for life unless not tolerated

#### Investigations prior to initiation of Hydroxyurea therapy:

- FBP - absolute neutrophil count (ANC) > 1,500/ $\mu$ l, platelet > 100,000/ $\mu$ l, Hb > 6g/dl.
- If Hb is less than 6gm/dl do Reticulocyte Count ***[Do not start hydroxyurea in patients with Hgb < 6 g/dl AND absolute reticulocyte count (ARC) < 100,000/ $\mu$ L]***
- Serum Creatinine - should be within normal range,
- Serum ALT – should not be greater than twice the upper limit of normal,
- Bilirubin Total and direct
- Urine Pregnancy Test in women
- HPLC - Quantification of HbF (if this test cannot be done, Hydroxyurea should be prescribed nevertheless and an elevated baseline HbF should not affect the decision to initiate hydroxyurea)

#### Dosage Initiation:

##### For adults:

- Start with **15 mg/kg/day** (round up to the nearest 500 mg); 5–10 mg/kg/day if patient has chronic kidney disease

##### For infants and children below 15 years of age:

- Start with **20 mg/kg/day** (in cases where only 500 capsules are available; calculate weekly dose in terms of number of capsules per week and distribute the required capsules throughout the week)

**Example:** a 10kg baby: Hydroxyurea initiated at 20mg/kg/day = 200mg/day = 1400mg/week = 3 capsules of 500mg/week hence Baby is given 1 capsule on Monday, Wednesday and Friday

**Note:**

Males and females of reproductive age should be counseled on the need to use contraception whilst on Hydroxyurea.

**Monitoring:**

Review the patient as follows: every 2 weeks for the first month; every month for the next 3 months; every 3 months thereafter.

For each review visit:

- Take history and do a physical examination. Assess adherence to Hydroxyurea and other medicines. Weigh patient every 3 months or whenever indicated and adjust dose accordingly
- Stop Hydroxyurea if ANC  $<1.0 \times 10^9/\text{L}$  OR Hb  $<6$  AND ARC  $<80$ ,  $\times 10^9/\text{L}$  OR platelets  $<80 \times 10^9/\text{L}$
- Do FBP once every 2 weeks for 1 month, every month for the next 3 months. If counts remain stable throughout the initial 4 months, FBP can be done once every 3 months going forward.
- In patients with fluctuating counts, FBP should be done monthly.
- Adjust Hydroxyurea dose to maintain ANC between  $1.5 - 2.5 \times 10^9/\text{L}$
- Increase the dose by 2.5 to 5mg/kg/day every 3 months if ANC  $>1.5 \times 10^9/\text{L}$ , Hb  $\geq 6 \text{ g/dL}$ , and platelet count  $>80 \times 10^9/\text{L}$
- Escalate to a maximum of up to 30mg/Kg in patients with abnormal TCD or stroke, or if ANC remains  $>1.5 \times 10^9/\text{L/uL}$ 
  - Check adherence before dose escalation.
  - Escalate by 2.5 to 5mg/Kg/day every 2 months (the minimum interval between dose increases is 2 months)
  - After each escalation check FBP according to initiation schedule
- Do serum Creatinine and Urea, ALT once every 6 months

**Dose adjustment for toxicity:**

If one or more blood count parameters fall into toxic range (ANC  $<1 \times 10^9/\text{L}$  or Platelets  $<50 \times 10^9/\text{L}$ ), stop hydroxyurea and do FBP every 2 weeks.

- Restart hydroxyurea at the same dose if affected blood count recovers in 2 weeks.

- Reduce hydroxyurea dose by 2.5 mg/kg if toxicity persists for more than 2 weeks or if there is a previous history of toxicity at the current dose.
- Do FBP according to the initiation schedule.

**Note:**

- 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.
- Use of hydroxyurea is associated with increase in haemoglobin level, HbF, and MCV
- Monitor RBC, MCV and HbF levels for evidence of laboratory response. HbF above 20% significantly improves clinical conditions. A lack of increase in MCV and/or HbF is not an indication to discontinue therapy
- Hydroxyurea therapy should be continued during hospitalizations or illness
- Do not start / initiate Hydroxyurea during episodes of severe illness, in such a situation wait until the patient has stabilized

**Contraindications:**

- Hydroxyurea should be discontinued in all pregnant women and breast feeding women
- Hydroxyurea should be stopped at least three months prior to conception in both males and females.
- Neurotoxicity - rare

**Side Effects of hydroxyurea:**

- Myelotoxicity
- Mouth ulceration
- Skin toxicity; rashes and hyperpigmentation

## **4. NUTRITION**

- Encourage exclusive breast feeding for the first 6 months of life. Complementary feeding should be introduced from 6 months with proteins, fruits, starches, and green leafy vegetables
- Thereafter, they should be encouraged to have a balanced diet. Choose a diet with a wide variety of foods from all food groups each day.

- Each day include items from: carbohydrates (e.g., yam, potato, rice, maize); Protein (e.g., legumes such as beans, milk, eggs, sardines, meat, fish, chicken); Vitamins and Minerals (Fruits and Vegetables ); Dairy products (e.g., milk, cheese); and, Fats and oils (e.g., Groundnuts, sunflower oil, palm oil, butter)
- During illness episodes, the appetite will be poor. If this occurs encourage frequent small feeds of a well-balanced diet
- Encourage all patients with SCD to drink plenty of water regularly, at least 3-4 litres/day in adults, in order to reduce the risk of dehydration, raised by hyposthenuria and nocturnal enuresis.
- Early involvement of dietitian/ nutritionist is essential for nutrition screening and assessment, which should include an ascertainment of malnutrition risk, an assessment for possible weight loss and nutrient deficiencies, and education and planning for the management of nutritional concerns

## **5. GROWTH AND DEVELOPMENT MONITORING IN CHILDREN**

- Serial growth measurements should be performed to capture both acute changes and long-term growth velocity
- Growth and development in children with SCD need to be monitored by measuring the following; a) Weight, ( every visit) b) Height (annually ), c) Mid-Upper arm circumference (MUAC should be >12.5cm from 1-5years
- Recumbent length for infants should be measured supine until 24 months of age; head circumference should be measured serially until an infant reaches at least 36 months of age
- Age-appropriate growth charts should be used to identify suitable trajectories in growth in infants, children, and adolescents, and identify suboptimal growth
- Parents/Caregivers should be educated that the children may have reduced weight and height when compared with their peers, but that may catch up in growth especially during adolescence.

## **6. EDUCATION AND PSYCHOSOCIAL COUNSELING**

- Educate all children from school going age with their parents/ caregivers and adults routinely about SCD at each visit: utilize available materials e.g., brochures, videos, and apps
- Talk to patients and parents, encourage them to talk about daily problems including finance and poverty, offer practical solutions

- Prompt patients and parents to talk about stigma and their experience with how their communities and others relate to them, dispel myths
- Educate parents/caregivers about importance of schooling, encourage their children to attend school when they are well and to keep a record of the number of school days lost
- Encourage adults to engage in economic activities
- Encourage patients to participate in social activities and not feel isolated
- Encourage participation in support groups where available
- Encourage self-care and reinforce health maintenance
- Ensure understanding of the importance of adherence to medical advice and treatment
- Offer psychoeducational sessions: individual and/or group or family sessions as appropriate

## **7. TRANSITION OF ADOLESCENTS TO ADULT CARE**

- Start preparation and plan the transfer at an early age (between 14 years and 15 years) in a developmentally appropriate manner.
- There should be a collaboration between pediatric and adult SCD health care providers to facilitate an effective transition
- Carry out a detailed review at various time points to evaluate knowledge and understanding about SCD, and readiness for transition.
- The paediatric health care providers should send a complete summary to the adult SCD health care providers.

## **8. TRAVEL MANAGEMENT**

- Individuals with SCD are not restricted to travel, however when traveling they should seek and adhere to traveling guidance / regulations depending on the area of travel e.g. immunization and other travel documents.
- Patient should be reminded to carry with them their SCD health passport and their routine medications
- Patients should be advised to keep warm when traveling to cold areas
- Patient should be advised on danger of acclimatizing to high altitude areas eg mountain climbing

## 9. ORGANIZING SUPPORT GROUP

- Suggest to patients and parents about setting up a support group if one is not available for them, they should also consider social media support groups
- Encourage patients and parents to organize their own groups but consider what healthcare or other professional support is required
- Help identify organizers/leaders for the group but emphasize that everyone has a role to play and can take turns, and be open to suggestions and contributions
- Consider how the group is structured e.g., parents of newborns and infants, teenagers only, group size and scope of support
- Consider the time and place to meet, frequency, length, cost of venue (free or cheap) eg. school, church, library or other public venue suitable and accessible for everyone, and available transportation
- Consider some ground rules and how to solve problems e.g., confidentiality, a person talking too much, someone who is upsetting others within the group, someone not well enough to attend and has responsibilities
- Consider fundraising and/or contribution from members towards sustainable running costs, refreshments, and social activities
- Consider whether to formalize the group after a while to become a registered charitable organization

## 10. REPRODUCTIVE HEALTH

### 10.1 Reproductive Counseling

- Provide educational and health promotion counseling to all women and men of childbearing age to reduce reproductive risk and improve pregnancy outcomes.
- If the partner of a man or woman with SCD has unknown SCD status, refer the partner for SCD screening.
- After testing, refer couples who are at risk for having a potentially affected fetus and neonate for genetic counseling.
- In women with SCD, regular use of contraception can decrease the health risks associated with unintended pregnancy.
- There is no contraindication for any of the usual contraceptives.

## 10.2 Pregnancy in SCD

### Pre-conception

Pregnancy in women with SCD is considered high risk. There is an increased risk of adverse pregnancy outcomes including intrauterine growth restriction, pre-term delivery and stillbirth.

- Risks to the mother include an increased frequency of pain crises and an increased risk of thrombosis, infections, preeclampsia, and death relative to women who do not have SCD.
- It is therefore important that a woman with SCD be seen prior to conception and be followed throughout pregnancy to improve outcomes for mother and baby.

Pre-conceptual counseling should include:

- Partner screening for haemoglobinopathy
- Analgesic dependency
- Transfusion history
- Immunization history
- Neonatal screening
  - Discussion of mode of delivery
- Hydroxyurea should be stopped at least three months before conception
- Folic Acid should be given once daily both pre conceptually and throughout pregnancy
- Where possible, women who have had a prior transfusion and anticipate pregnancy should be tested for red cell alloantibodies. If present, the partner should be tested for the corresponding antigens and if also positive, they should be counseled on hemolytic disease of the newborn and how it is managed. A plan should be made to make sure appropriate matched blood is available in case she needs blood transfusion (extended blood typing is preferred).

### Pregnancy

- Refer to a high-risk antenatal clinic for follow up
- It is important to ensure that each patient has an individualized care plan, clinic visits should be regular, preferably every 6 to 12 weeks.
- Prescribe routine antenatal vitamins.

- Offer a viability scan at 7 - 9 weeks of gestation, a routine first trimester scan (11 - 14 weeks gestation), and a detailed anomaly scan at 20 weeks gestation
- ECHO if possible to screen for pulmonary hypertension
- Pregnant women with SCD should be considered for low dose aspirin 75mg once daily from 12 weeks of gestation
- Consider use of venous thromboembolism prophylaxis for patients with additional risk factors for VTE e.g., previous history of VTE, caesarean section or immobility.
- Persistent vomiting with dehydration increases the probability of sickle cell crisis; therefore they should be advised to seek medical attention early.
- Prophylactic blood transfusion is not recommended

### **Intra-partum management**

- Pregnant women with SCD who have a normally growing fetus should be offered elective birth through induction of labor, or by elective caesarean section if indicated, after 38+0 weeks gestation
- Blood should be cross-matched and transfused if indicated
- Women who have had hip replacements secondary to AVN, should have discussions on suitable positions for delivery
- Maintain adequate hydration, warmth and Oxygen saturation >94% during delivery
- Regional analgesia is recommended for caesarean section
- Avoid pethidine, but other opioids can be used

### **Post-partum management**

- Counsel about the use of contraception
- Assess and manage neonatal opioid dependency and withdrawal all neonates with history of in utero opioid exposure

## **11. EARLY DIAGNOSIS THROUGH NEWBORN SCREENING (NBS)**

- Early diagnosis through Newborn Screening (NBS) or Early Infant Diagnosis (EID) for SCD and provision of comprehensive care can reduce under-five (U5) deaths due to SCD by 90%.
- Newborn screening for SCD is usually done within 24 hours of delivery in postnatal wards.

- Early infant diagnosis for SCD can be done at RCH clinics when babies are brought in for routine vaccinations at 6, 10 and 14 weeks of age.
- This will still allow early initiation of essential interventions to reduce morbidity and mortality among children identified to have SCD.
- NBS/EID for SCD is done by collecting blood on a dried blood spot (DBS) from a heel prick.
- The DBS cards are then sent to the laboratory for testing using isoelectric focusing (IEF) or High-Performance Liquid Chromatography (HPLC) or by point of care test such as Sickle SCAN or Hemotype SC.
- Results should be ready within 2 – 4 weeks from DBS collection.
- Repeat test should be done from three months of age to confirm the diagnosis of SCD.

**Mechanisms should be in place to inform parents of babies with SCD disease about the screening results so that they can bring their babies for early initiation of interventions (Folic acid, Pen V, vaccination, malaria prevention, early identification and treatment of complications).**

## **12. PERI-OPERATIVE CARE IN SCD**

Perioperative complications of surgery in SCD patients include hypoxia, dehydration, painful crisis, severe anaemia, and acute chest syndrome.

Good surgical and anesthetic expertise and experience is important when undertaking surgical procedures in SCD patients.

Do laboratory tests; FBP, renal and liver function test, serum electrolytes, blood grouping and cross matching.

Give blood transfusion to achieve a preoperative Hb level of 10g/dL. Monitor temperature, heart rate, hydration status and oxygen saturation > 95% throughout the surgery and 48 hours after surgery.

Strategies to improve perioperative outcomes in SCD include conservative preoperative blood transfusion, epidural analgesia, and adequate postoperative pain control with opiate and non-opiate analgesia, give prophylactic antibiotics as required, encourage early ambulation, assess post-operative lab results and monitor for potential complications e.g. acute chest syndrome.

## 13. SCREENING FOR SPECIFIC CONDITIONS

### 13.1 Screening for Renal disease

All individuals with SCD aged 10 years and above should be screened for proteinuria.

- If the result is negative, screening can be repeated annually
- If positive, then perform a first morning void urine albumin-creatinine ratio, 24 hour urine creatinine clearance and if abnormal, refer to the next level facility with adequate expertise.
- For patients with albuminuria (albumin-creatinine ratio  $\geq 3.5$ mg/mmol) target Blood pressure (BP)  $\leq 130/80$ mm/Hg
- If BP is above 130/80 in the presence of proteinuria initiate treatment with Angiotensin converting Enzyme (ACE) inhibitors or Angiotensin receptor blocker (ARB) or calcium channel blocker.
- In the absence of proteinuria initial treatment should be with calcium channel blocker.

### 13.2 Screening for Cardiovascular Diseases

- All adults (greater than 18 years) with SCD should have a baseline echocardiogram, and every three to five years if results remain normal.
- Children with symptoms suggestive of heart diseases should be evaluated for cardiac diseases.
- Routine echocardiogram is not necessary in children with no symptoms suggestive of cardiac diseases.
- Routine Electrocardiogram (ECG) is not recommended in patients with SCD.
- Screen for hypertension and treat to lower systolic blood pressure  $\leq 140$  and diastolic blood pressure  $\leq 90$

### 13.3 Screening for Pulmonary Hypertension

- All patients must do ECHO annually to screen for Pulmonary Hypertension
- If pulmonary arterial pressure (PAP) is  $>40$ mmHg or tricuspid regurgitation jet velocity (TRV) is  $>2.5$ m/sec or NT-proBNP is  $>164.5$ pg/mL and/or low 6MWD is  $\leq 333$ m do confirmatory test (right heart catheterization)

- Excluding other associated conditions such thromboembolic disease, iron overload, systemic hypertension, obstructive sleep apnea, and chronic hypoxemia must be ruled out and treated.
- Management: Persons with pulmonary hypertension should be co-managed by cardiologist or pulmonologist and hematologist.

### 13.4 Screening for Retinopathy

- All children with SCD aged 10 years and above should be referred to an ophthalmologist for a dilated eye examination.
- If normal, re-screen at 1-2 years intervals.

### 13.5 Screening for risk of stroke using Neuroimaging

- Annual screening with Trans cranial Doppler (TCD) ultrasound from 2 years to 16 years
- In children with conditional (170–199 cm/sec) or elevated (>200 cm/sec) TCD results, refer to a specialist with expertise in chronic transfusion therapy aimed at preventing stroke
- All patients with abnormal TCD should be given the **maximum tolerated** dose of Hydroxyurea (not exceeding 35mg/kg/day for adults and 30mg/kg/day for children)

## PART V: OUTPATIENT MANAGEMENT OF SCD

### **The Aim of the SCD clinic is to:**

- Establish baseline observations for comparison in acute illness
- Educate parents/children in the management of SCD and its complications
- Provide genetic counseling to parents with regards to SCD and adolescents with SCD
- Monitor the medical, educational and psychosocial development of patients with SCD
- Provide appropriate prophylactic care to patients to avoid exacerbations of disease
- Make timely interventions when exacerbation or complications occur
- Patients in steady state should be given 3 months supply of their routine medications

### **Appointment frequency:**

|                                                       |          |
|-------------------------------------------------------|----------|
| 0-5 years old                                         | 3months  |
| ≥ 5 years old                                         | 3 months |
| PRN for medical, educational or psychosocial concerns |          |

### **Prophylaxis against pneumococcal and other infections**

There is very good evidence that penicillin prophylaxis protects against encapsulated bacterial septicemia / meningitis *provided it is taken regularly*. It is essential that all children with sickle cell disease take penicillin twice daily continuously (or erythromycin, if penicillin sensitive), starting by the age of 3 months until the age of 5 years. Stress to the parents the importance of giving it continuously and keep this under review.

### **Penicillin V Dosage according to Age**

| Age             | Dosage           |
|-----------------|------------------|
| Less than 1year | 62.5mg 12 hourly |
| 1-3 years       | 125mg 12 hourly  |
| Above 3 years   | 250mg 12 hourly  |

### **Erythromycin Dosage according to Age**

## 1. THE NEW PATIENT APPOINTMENT

Patients are usually referred to SCD clinics following a recent diagnosis. For the new patients, do the following;

### **Obtain a full history which includes:**

- Birth history - including mother's antenatal, natal and post-natal history
- Immunization history - ask to see documentation
- Dietary history
- Developmental history including schooling and school attendances (be aware that subtle problems in development may be due to silent stroke)
- Medical history – include number, frequency and types of crises, previous admissions and hospital visits
- Transfusion history
- Medication
- Allergies
- Family and social history - include names and date of birth of siblings, haemoglobinopathy status, as well as family's previous experience of SCD

### **Perform thorough physical examination including:**

- SpO<sub>2</sub>
- Height, Weight and Occipital Frontal Circumference (OFC) in infants
- Mid-parental height estimation
- Pubertal evaluation (if appropriate)

### **Do blood tests (delayed in babies until >6 months old):**

- COMPLETE BLOOD COUNT (CBC), reticulocyte counts and film
- G6PD assay if available
- RFT, electrolytes, LFTs
- Blood Grouping
- Hepatitis B Ag and Ab
- Consider HCV and HIV Ab screen

### **Discuss:**

- Diagnosis and its implications
- Acute complications in infancy including dactylitis, acute splenic sequestration

- Other complications as relevant
- SCD Health Passport and explain how to use it
- Medication adherence
- follow up clinic attendance
- Vaccinations

**Provide / Organize / Prescribe:**

- SCD Health Passport
- Contact details of the patient. Telephone and residence.
- Instructions on how to examine an enlarged spleen / liver and what to do.
- Genetic counseling: plans for future children can be discussed
- Penicillin V, hydroxyurea and Folic acid
- Referral to any other specialist as required
- Follow-up appointment

## **2. THE FOLLOW-UP CLINIC**

Not all of the following needs to be done on each attendance. Always check that the patient has had everything done on the new-patient list; due to the nature of a new-patient attendance it is not always possible to have achieved everything at that first appointment.

**History should include:**

- Immunization
- Diet
- Developmental progress (be aware that subtle problems in development may be due to silent stroke)
- School attendance and achievement; ask to read reports and ask parents/caretakers about school progress
- Snoring / sleep apnoea, consider ENT referral
- Other problems including enuresis
- Medication – including doses and type of analgesics used at home
- Allergies
- Family history - note any changes e.g. Siblings etc.
- Social cultural History – including job, housing
- Medical history – include number, frequency and types of crises

**Examination, full and thorough, includes:**

- Pulse, blood pressure, respiratory rate, SpO<sub>2</sub>
- Height and weight (OFC in <2yr olds)
- Presence of pallor and jaundice
- Document spleen and liver size
  
- Neurological examination
- Other systems examination as appropriate
- Pubertal staging (as appropriate, when >10yr old)

**Blood tests: at each visit**

- FULL BLOOD COUNT, reticulocytes count and film
  
- Malaria test if history of fever or febrile (T>37.5°C)
- RFT, electrolytes, , LFTs when necessary to check for signs of haemolysis
- Blood Group and Save – if not already done
- HBV, HCV, HIV antigen / antibody if previously transfused
- Hepatitis B antibodies if vaccinated
- Other investigations as clinically indicated

**Do the following**

- Document COMPLETE BLOOD COUNT/ Hemoglobin level results in SCD health passport.
- Give Penicillin V, hydroxyurea and Folic acid
- Check Vaccinations if not up-to-date
- Arrange for Annual TCD from age 2 -16 years
- Ensure education on sickle cell disease and its complications is provided (with every visit)
- Reinforce advice on healthy diet, nutrition, hydration, hygiene, prevention of crises and lifestyle choices
- Ensure parents / patients are aware of complications (esp. boys with priapism)
- Discuss therapeutic options such as transfusion.
- Involve psychosocial counselors *when there are concerns about developmental or cognitive abilities and or if there are particular difficulties in coping with illness*
- Arrange for transition to adults clinic from 14 -15 years old
- Give appointment for next clinic visit

### 3. TREATMENT PRESCRIBED IN CLINIC VISITS

| Drug                             | Dose: Adult                             | Dose: Child                                                                                  |
|----------------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------|
| Penicillin V                     | Not given                               | <1yr 62.5mg BD<br>1-3yrs 125mg BD<br>>3yrs 250mg<br>> 5 yrs not usually given as prophylaxis |
| Folic acid                       | 5mg or 1mg as available OD              | <1yr 1.25mg OD<br>1-3yrs 2.5mg OD<br>>3yrs 5mg OD                                            |
| Analgesia for PRN use            | Paracetamol 1g QDS, Ibuprofen 400mg QDS | Paracetamol 15mg/kg QDS, Ibuprofen 5mg/kg TDS                                                |
| Mebendazole after every 3 months | 400mg stat dose                         | 1-2years - 200mg<br>■ 2years - 400mg                                                         |

### 4. LABORATORY DIAGNOSIS IN SCD

All children presenting with unexplained acute illness, including acute pain in any part of the body, anaemia, acute neurological symptoms, loss of vision, collapse, respiratory symptoms, hepatosplenomegaly, jaundice, swollen limbs and sepsis should be tested for SCD.

Screening Tests for SCD include:

- Sickling Test
- Sickle Solubility Test.

Confirmatory Tests for SCD include;

1. Approved Point of Care (POC) diagnostic tests
2. Gazelle Hb Variant
3. Iso Electric Focusing (IEF)
4. Haemoglobin electrophoresis
5. HPLC (High -Performance Liquid Chromatography)

Other ancillary laboratory investigations useful in detection and monitoring of the disease include:

- FBC - Red cell indices may suggest macrocytosis due to increased reticulocytosis or compliance with hydroxyurea therapy
- Reticulocyte count - usually ranges from 5 to 15% in sickle cell disease

- Peripheral blood film - findings may include irreversible sickled red cells, polychromasia, occasional nucleated red cells, and schistocytes, as well as Howell-Jolly bodies. Target cells may also be seen.
- Biochemical changes include high LDH, low haptoglobin, high total and indirect bilirubin, and high AST.
- Genetic studies such as PCR are used for prenatal and preimplantation diagnosis

## **PART VI: BLOOD TRANSFUSION IN THE MANAGEMENT OF SICKLE CELL DISEASE**

Blood transfusion is a key therapeutic modality in SCD. Overall 60% of patients with sickle cell disease receive a transfusion during their lifetime. All staff involved with the prescription and administration of blood and blood products must be familiar with the NBTS transfusion guideline.

There are three main types of transfusion and rationales of transfusing sickle cell patients

- Acute simple transfusion.
- Exchange transfusion, Manual/Automated erythrocytapheresis
- Chronic top up transfusion

### **1. ACUTE SIMPLE TRANSFUSION**

In acute simple transfusion, a patient receives a transfusion with the purpose to increase the patient's red blood cell mass, oxygen carrying capacity and also decrease the percentage of HbS.

Indications for acute simple transfusion:

- Severe anaemia < 5g/dl with symptoms
- Drop in Hb > 2g/dl from normal steady-state (baseline) value with symptoms
- Acute Splenic sequestration (moderate or severe)
- Acute Chest Syndrome with low Hb (e.g. < 8 g/dl)
- Stroke
- Mesenteric/girdle syndrome

### **2. CHRONIC TOP UP TRANSFUSION**

In chronic top transfusion patients receive a long term PRBC transfusion with the purpose to suppress endogenous erythropoiesis, maintain the HbSS level < 30% (depending on the clinical situation) and thus prevent certain complications of sickle cell disease. This can be achieved by regular top up transfusions keeping the Hb between 10-11g/dl, typically every 4-6 weeks.

Indications of chronic top transfusion in Sickle cell patients

- Secondary stroke prevention. History of previous stroke (CVA).
- Primary Stroke prevention. History of high risk patients based on elevated Transcranial Doppler ultrasound (TCD) and/or diffusion/perfusion MRI/MRA.
- Multiple, severe episodes of acute chest syndrome
- Intractable or very frequent severe episodes of painful crises (at least 6 admissions in past year).
- Chronic lung disease secondary(pulmonary hypertension) due to episodes of acute chest syndrome
- Presence of organ failure such as chronic renal failure
- Chronic leg ulcers,
- Recurrent priapism

Dosage for top up transfusions-The volume of blood required (ml) is given as follow:  
 $(\text{Hb desired}(10\text{g/dl}) - \text{Hb current}(\text{g/dl}) \times \text{Weight (kg)} \times 4 = \text{Volume needed (mls)}$

Investigations to be performed to patients on chronic transfusion

- FULL BLOOD COUNT
- HbSS % level (annually)
- Cross-match (ensure that extended RBC phenotype is already known)
- Serum Ferritin levels after 20 units of blood; if  $>1000\text{mmol/L}$  consider iron chelators or switch to exchange blood transfusion. (Always interpret ferritin results in the presence of CRP results)
- Serum HBsAg and level of anti-HBs Ab, vaccinate against Hep B (revaccinate if titres  $< 100 \text{ IU/ml}$ )
- Serum HCV Ab and HIV.

Do not attempt to raise the hemoglobin by more than 4 g/dl at any one transfusion. The usual rate of transfusion is 2-3ml/kg/hour and for elective transfusion should never exceed a maximum rate of 150 ml/hour. Post-transfusion; check FULL BLOOD COUNT and HbA/S ratio.

### 3. EXCHANGE TRANSFUSION

Exchange transfusions are performed by removing the patient's own blood and replacing it with an equal volume of transfused donor PRBCs and normal saline. Exchange transfusion aims to rapidly reduce the

percentage of sickle cells in the circulation when a patient develops a life-threatening complication of the disease. It is not to be undertaken lightly, as the possibility for complications are considerable. Exchange transfusion can be through manual or automated procedure. The purpose of an acute exchange transfusion is to reduce the percentage of RBCs that contain hemoglobin S (i.e., reduce the “percent sickle”) to 30%.

Indications for Exchange Transfusion:

- Suspected new acute stroke or transient ischemic attack (TIA)
- Prevention of secondary stroke
- Severe Acute chest syndrome: symptomatic patient (hypoxia with low or falling PaO<sub>2</sub>, respiratory distress), episode involving multiple lobes, not responsive to simple transfusion
- Preparation for surgery, prior to general anesthesia in patient with high baseline Hb (e.g. Hb SC disease) or h/o severe ACS or pulmonary disease
- Intractable priapism (> 4 hours) unresponsive to pharmacological therapy.
- Pregnant women with intractable VOC.
- Multi-organ failure e.g. associated with systemic fat embolism

### **Procedures for Manual Exchange Blood Transfusion**

A “one-volume” or full volume exchange is the usual procedure and should reduce the patient’s % HbS by approximately 60-70%. Calculations (for manual exchange):

- Total volume = 80ml/kg
- Volume of PRBC = 50ml/kg
- Volume of NS= 30ml/kg

Aim

- To reduce the HbS% level to < 30% over 2 - 3 days if acutely ill, when more rapid exchange may be appropriate.
- To keep Hb < 10g/dl initially and by the end of the procedure (or at steady state level in those with higher baseline Hb, e.g. HbSC patients with Hb of 11-12 g/dl)
- To maintain a steady state blood volume and Hb throughout the exchange

**Exchange transfusions should be undertaken by experienced medical and nursing staff and should not be initiated without discussion with the responsible paediatric and hematology consultants**

### Type of Blood required for transfusion in Sickle cell patients

- When transfusing SCD patient, use packed red blood cells (PRBCs) that are
- Leukocyte-reduced/filtered
- Sickle hemoglobin (HbS) negative, and
- Phenotype/antigen matched.
- All SCD patients should have an extended RBC phenotype performed, preferably between 6 and 12 months of life and before the first blood transfusion. An extended red cell antigen profile includes Rh (C, E or C/c, E/e) and Kelly. This phenotype should become a part of the permanent blood bank record then PRBC transfusions should be matched to minor antigens as thoroughly as possible to prevent alloimmunization. This is essential for patients needing chronic or repeated transfusions and for those with a history of alloantibody.
- The use of leukocyte-reduced/filtered blood is intended to reduce the risk of allosensitization to leukocyte-related antigens in multiply-transfused patients. Filtration is the best means of leukocyte-depleting blood.

### **General Principles:**

- Patients must be well hydrated prior to starting an exchange transfusion. Adequate explanation must be given to the child and parents as to the indication for exchange and its potential risks and benefits and this should be documented in the notes
- Principles of asepsis should be maintained throughout the procedure (closed circuit).
- Record output and input on the exchange transfusion record chart
- Do not use diuretics
- Continue to administer intravenous fluid at the standard rate between exchange transfusion cycles to keep child well hydrated
- Critically ill patients may require exchanges to be more frequent than daily
- If possible, leave a 4 - 8 hour break between exchanges
- Pay particular attention to PaO<sub>2</sub>, CVP, acid base balance, urea, electrolytes, Ca<sup>++</sup>, Mg, core temperature and clotting in sick patients
- Exchange transfusion should be an isovolaemic procedure and exchanges should be done in aliquots of approximately 5ml/kg (do not exceed 10ml/kg aliquots)

- The Hb should be <10g/dl to reduce the risk of hyperviscosity - stroke
- Continue with exchange procedures until the HbS < 30%

### **Preliminary investigations:**

- FULL BLOOD COUNT
- HbS % level (not urgent at first exchange)
- Cross match approximation 30mls/kg (average unit contains 220 -250mls)
- Request exchange transfusion blood from laboratory. It will need to be ABO, Rh and Kell matched and sickle negative
- Urea, electrolytes, creatinine, liver function tests, Ca<sup>++</sup>
- Arterial blood gases in those with symptoms suggestive of ACS or girdle syndrome
- Save serum for Hepatitis B and C and HIV, if not done recently

### **Volumes required:**

Exchange transfusion in children requires a total exchange of 1.5 - 2 times their blood volume, performed as 3 or 4 exchanges. Usually, equal volumes is venesected and transfused, but must replace venesected blood as  $\frac{1}{3}$  saline and  $\frac{2}{3}$  packed cells to keep haematocrit stable.

Volume (ml) exchanged in each procedure can be calculated as:

**(Desired Hb g/dl - Pre Treatment Hb g/dl) x (weight in kg) x 3 = vol. of blood in ml x 100**

For older patients (>50kg), the volume of blood required can be calculated by:

**(Desired Hb - Pre Treatment Hb units) = units of blood; maximum 4 units per transfusion**

**Note: desired Hb is normally 10g/dl**

### **Example Calculations:**

*25 kg Child, starting Hb = 7g/dl, desired Hb=10g/dl @ 30ml/kg = ((10-7)\*25) \* 100*

*= 750mls blood required.*

*Request 4 units for exchange (each unit is 220 – 250 mls)*

### **Vascular access:**

- 2 ports of venous access are required: one for venesection, the other for administering blood and saline. In certain cases an arterial line may be used for venesection.

- Uses of two larger lines are optimal (16-18gauge).

#### **Observations:**

- Pulse, respiratory rate, BP and SaO<sub>2</sub> every 15 minutes
- Temperature hourly
- May require laboratory monitoring during exchange if clinically indicated may also require monitoring of electrolytes and glucose.

#### **Possible immediate complications**

- Transfusion Reaction
- Tetany / twitching
- High Hb may cause sludging, worsening the sickling process. May cause cerebral sludging particularly in patients with prior CNS problems
- Hypertension in patients with circulatory overload. If diastolic BP increases by > 20 mmHg above baseline recording, monitor blood pressure hourly.

### **4. COMPLICATIONS OF BLOOD TRANSFUSION**

SCD patients are prone to suffer from all the complications related to blood transfusion including both acute and chronic complications. However, Delayed Haemolytic Transfusion Reaction (DHTR) is increasingly becoming prevalent because of the risk posed by multiple transfusion and alloimmunisation. DHTR is defined as a significant drop in the haemoglobin within 21 days post transfusion associated with one or more of the following;

- New red cell alloantibodies
- Haemoglobinuria
- Accelerated HbS% increase with concomitant fall in HbA% post transfusion,
- Relative reticulocytopenia or reticulocytosis from baseline,
- Significant LDH rise from baseline,
- Exclusion of an alternative cause.
- Management;
- Provide immunosuppressive therapy; Prednisolone 1-2 mg/kg (maximum 60mg/day) followed by a very slow tapering (weeks) to prevent rebound vasso-occlusive pain events. Alternatively Methyl-prednisolone 0.5g daily up to 5 days in adult patients can also be used.

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