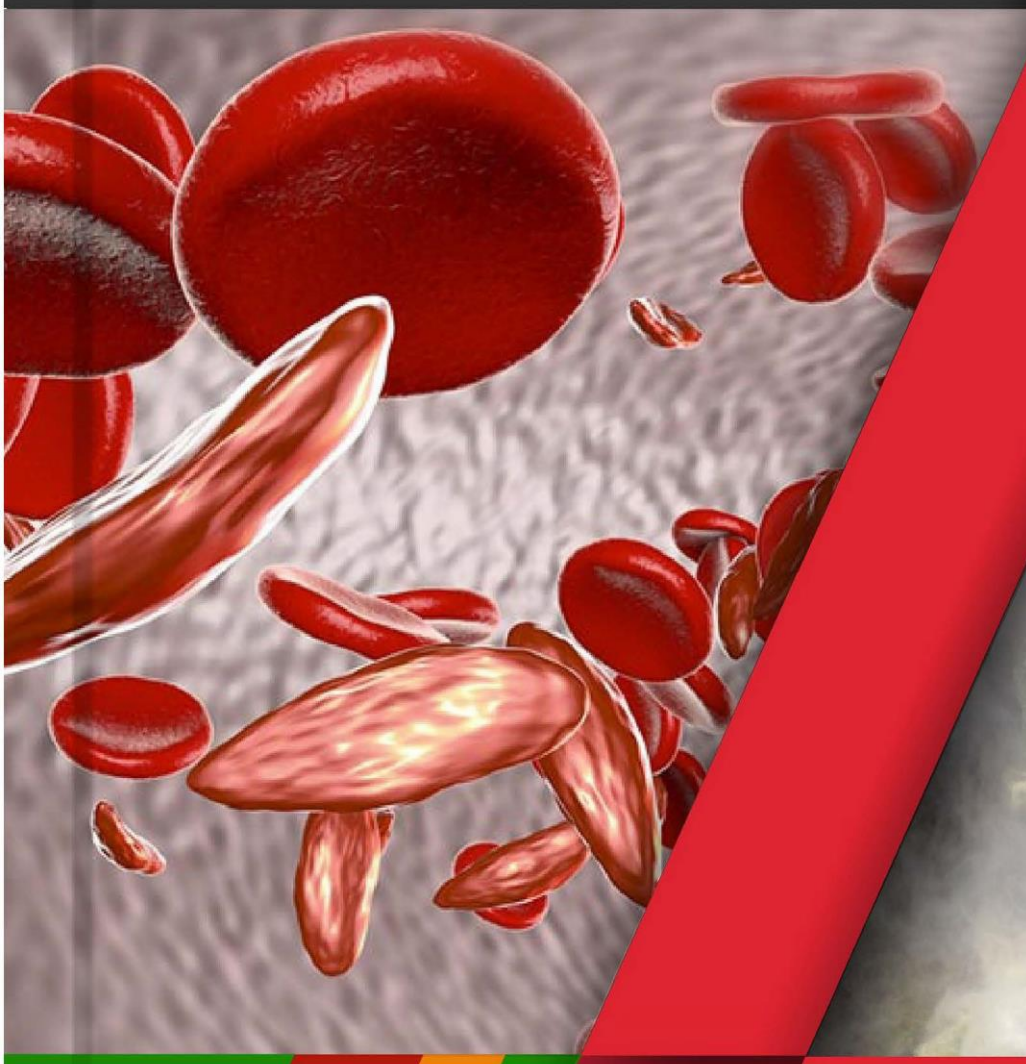
GUIDELINES

For the Management of SICKLE CELL DISEASE IN ZAMBIA



REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH

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FOREWORD

The guidelines for the Management of Sickle Cell Disease (SCD) in Zambia have come at a time when the Ministry of Health and all its partners have put premium on the attainment of Universal Health Coverage (UHC) 'leaving no one behind'. Though the actual prevalence of the disease in the country is unknown, available data indicates that the burden of Sickle Cell Disease in Zambia is huge, and that UHC would remain a pipe dream if the plight of the many affected people is not adequately addressed.

These guidelines are the first edition and seek to streamline and standardise sickle cell disease care in the country. They also provide comprehensive information for clinicians and other health care providers, for appropriate management of sickle disease across the continuum of care, and across the life course. The guidelines consider evidence based best practices of international standards which, if applied, will no doubt be a game changer in the lives of our people with Sickle Cell Disease.

The sickle cell guidelines are intended to fill a void which has been there in the care of sickle cell disease patients. They are not meant to be a prescription but a guide which will be revised from time to time as new evidence-based knowledge emerge. With standardisation of Sickle Cell disease management and registration of persons with Sickle Cell disease, it will be possible to have a cohort on which research activities could be conducted to improve the quality of life of persons

Whilst UTHs have had structured sickle cell care for a long time, with the massive recruitment of health care workers including distribution of specialists, most health facilities have started setting up dedicated clinics for sickle cell patients.

It is therefore my hope that the care for sickle cell patients will continue to improve and all patients will receive the minimum acceptable package of care for their illness across diverse clinical settings regardless of where they are being managed from.

Dr Chitalu Chilufya, MP
MINISTER OF HEALTH

ACKNOWLEDGMENTS

I wish to express my special appreciation to the group of experts comprising the Sickle Cell Taskforce for their dedication and hard work to see this document to completion despite their busy schedules.

I am also grateful to all our cooperating partners for the financial and technical support rendered to the taskforce during the development of these guidelines.

Dr Kennedy Malama
Permanent Secretary – Technical Services
MINISTRY OF HEALTH

Professor Chifumbe Chintu
1935-2017

These guidelines are dedicated to Professor Chifumbe Chintu who spear-headed this work and dedicated his life to improving the medical care and quality of life of patients with sickle cell disease and other blood disorders.

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ACRONYMS AND ABBREVIATIONS

ACS	Acute Chest Syndrome
ANA	Antinuclear antibodies
AVN	Avascular necrosis
BMT	Bone marrow transplant
BT	Blood transfusion
BP	Blood pressure
CNS	Central nervous system
CRP	Complement reactive protein
CT	Computerised tomography
CXR	Chest X-ray
DAT	Direct Antiglobulin test
DBS	Dried blood spot
EEG	Electroencephalogram
ESR	Erythrocyte sedimentation rate
ESRD	End stage renal disease
FBC	Full blood count
GCS	Glasgow coma scale
Hb	Haemoglobin
HCV	Hepatitis C virus
HbS	Haemoglobin S
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
HPLC	High performance liquid chromatography
HSCT	Haemopoietic stem cell transplant
HU	Hydroxyurea
IEF	Isoelectric focusing
IVP	Intravenous pyelogram
LFTs	Liver function tests
LDH	Lactate dehydrogenase
LP	Lumbar puncture
LMWH	Low molecular weight heparin
MPS	Malaria parasite slide
NEJM	New England journal of medicine
OD	Once daily
Plt	Platelet
pRBC	Packed Red Blood Cells
PS	Peripheral smear
RBCs	Red blood cells
RF	Rheumatoid factor
SCA	Sickle cell anaemia
SCD	Sickle cell disease
Retic	Reticulocyte count
TRCA	Transient red cell aplasia
U&Es	Urea and electrolytes
VOC	Vaso-occlusive crisis
WBC	White Blood Cells
X-match	Cross match

CHAPTER 1: INTRODUCTION

Sickle Cell Disease (SCD) in Zambia was first described by Beet in 1946 while working in Balovale district (now Zambezi District) in which it was observed that there was a high incidence of the sickle cell trait particularly amongst children. In 1972 Barclay described the distribution of the sickle cell trait in Zambia showing the highest incidences of the trait to be in the northern regions of Zambia. It was further observed that the incidence was higher in the rural populations than in the urban populations. The disease has since been reported in all districts of Zambia

The SCD trait is estimated at 18% of the Zambian population. The University Teaching Hospitals, Lusaka, with the largest population of SCD patients, has on its records over 6, 000 patients currently registered with them. The majority of these are children below the age of fifteen years. SCD patients accounted for 12% of the total all- cause admissions at the UTH- Children's Hospital in 2017 and yet SCD was 4th of the top five causes of mortality among children admitted to UTH- Children's Hospital in 2017 and top 10 among the causes of seeking medical attention.

Definition: SCD is a major genetic disease in most Sub-Saharan countries in Africa. It is a haemoglobinopathy characterised by inheritance of 2 abnormal genes coding for the formation of haemoglobin, one of which is sickle haemoglobin or haemoglobin S (HbS). SCD denotes all genotypes containing at least one sickle haemoglobin gene in which HbS makes up at least half the haemoglobin present. In sickle cell anaemia (SCA) both genes make HbS resulting in all the haemoglobin being sickle haemoglobin. The SCA genotype is denoted HbSS. In addition to SCA, there are five other compound heterozygous conditions which can occur:

- Haemoglobin S/ Haemoglobin C(HbSC)
- Haemoglobin S/ß thalassaemia (HbSß+ and HbSß0)
- Haemoglobin S/ Haemoglobin OArab (HbSOArab)
- Haemoglobin S/ Haemoglobin D-Punjab (HbSDPunjab)
- Haemoglobin S /Haemoglobin Lepore (HbSδß)

Pathophysiology of the disease: A single nucleotide substitution in the sixth codon of the ß globin gene results in the substitution of valine for glutamic acid on the surface of the variant ß-globin chain. This change allows HbS to polymerise when deoxygenated and is the primary event in all sickle cell pathology. The polymer is a rope-like fibre that aligns with others to form a bundle, distorting the red cell into characteristic sickled forms. These deformed sickle red cells can occlude the microvascular circulation producing vascular damage, organ infarcts, painful episodes and other symptoms associated with SCD. The deformed red cells have a shorted life span and are rapidly haemolysed. These are the two cardinal pathological processes: haemolysis and vaso-occlusion.

SCD is a major public health concern particularly in Africa with the majority of afflicted children dying before the age of five, usually from an infection or severe anaemia. The survivors remain vulnerable to exacerbations of the disease. There is sufficient evidence that neonatal screening for SCD, when linked to timely diagnostic testing, parental education and comprehensive care, markedly reduces morbidity and mortality in infancy and early childhood. The simple, inexpensive and cost-effective interventions such as teaching mothers to palpate the spleen, prophylactic penicillin, folate and antimalarial to prevent infections, anaemia and malaria are not available to most patients, because they are not diagnosed in the first place.

Presently, the only cure for SCD, which is Haemopoietic Stem Cell Transplant (HSCT) is not accessible and affordable to the majority. However, cost-effective treatment exists for the pain and other aspects of the disease. The most important components of this treatment are early intervention with analgesics, antibiotics, rest, good nutrition, folic acid supplementation and high fluid intake.

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CHAPTER 2: EPIDEMIOLOGY OF SICKLE CELL DISEASE

Sickle Cell Disease (SCD) predominates in Africa. In several sections of Africa, the prevalence of sickle cell trait is as high as 30%. Although the disease is most frequently found in sub-Saharan and Western Africa, it is also found though with much less frequency, in eastern Mediterranean, Middle Eastern population and India, all of which have areas in which malaria is endemic. Its prevalence varies but is high in these countries because of the survival advantage to heterozygotes in regions of endemic malaria. However, as a result of migration, both forced and voluntary, it is now found worldwide. The World Health Organization estimates that 7% of the world's population carries a haemoglobin mutation and that 300,000 to 500,000 children are born each year with severe hemoglobinopathy

Nigeria alone has been estimated to have at least 150,000 babies born with SCD annually. In the Democratic Republic of Congo and India SCD affects up to 2 percent of the population, and the carrier prevalence rate (sickle cell trait) is as high as 10 to 30 percent. Prevalence levels decrease to between 1% and 2% in North Africa and to less than 1% in Southern Africa. In countries such as Cameroon, Republic of Congo, Gabon, Ghana and Nigeria, the prevalence is between 20% and 30% while in some parts of Uganda it is as high as 45%. In countries where the trait prevalence is above 20% the disease affects about 2% of the population. The geographic distribution of the sickle-cell trait is very similar to that of malaria. The sickle cell trait has a partial protective effect against malaria, and this may explain why it has been maintained at such high prevalence levels in tropical Africa. Those who inherit the gene from both parents do not have this protection. In addition, they suffer from severe effects of SCD and may die before they reach reproductive age.

The SCD trait is estimated at 18% in the Zambian population. The University Teaching Hospitals, Lusaka, with the largest population of SCD patients, had on its records over 6, 000 patients registered with them as of end of 2019. The majority of these are children below the age of fifteen years. SCD patients accounted for 12% of the total all- cause admissions at the UTH- Children's Hospital in 2017. In addition, SCD was 4th of the top five causes of mortality among children admitted to UTH- Children's Hospital in 2017 and top 10 among the causes of seeking outpatient care.

In a small cross-sectional study in Chitambo area, in central province of Zambia, in 2017 during an outreach program 503 children aged 3 months to 18 years were screened for SCD. Of the screened individuals, analysis of the dried blood samples revealed that 78 had sickle cell trait and 17 had SCD, a prevalence of 15.5% and 3.4%, respectively.

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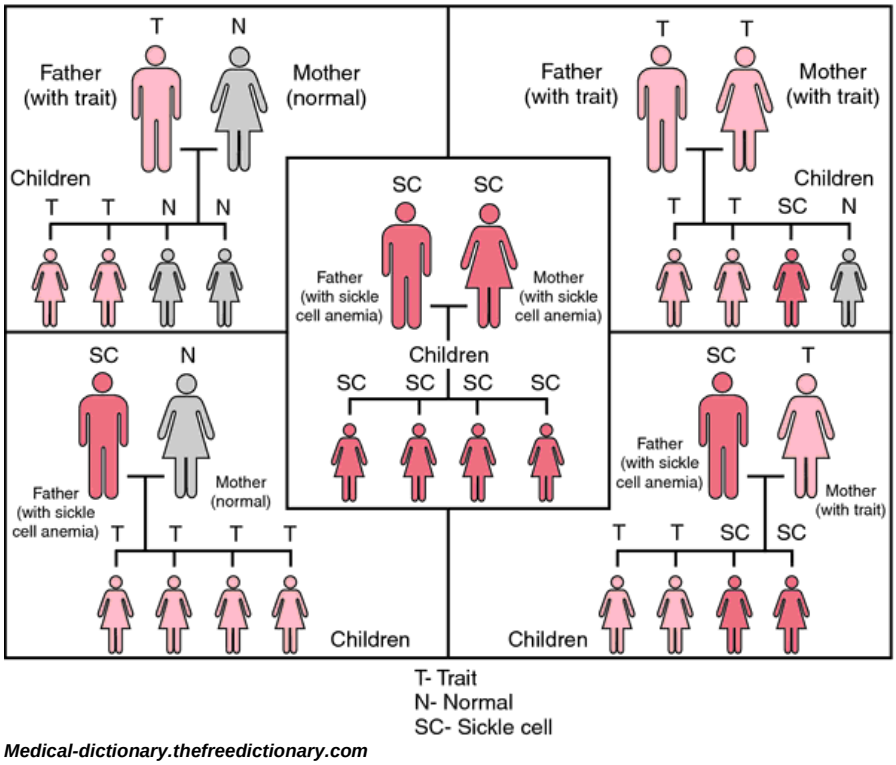
CHAPTER 3: INHERITANCE OF SICKLE CELL ANAEMIA

Sickle cell anaemia (SCA) is a hereditary disease of the haemoglobin found in the red blood cells (RBCs). It is inherited from both parents, in an autosomal recessive manner. Both parents have a defective gene which is passed on to the affected children. SCA is characterised by inheritance of 2 abnormal genes, both of which code for HbS (Figure 3.1). SCA occurs when one is homozygous for HbS or (HbSS) and constitutes one of the severest forms of SCD. It is the prevalent variant of SCD in sub-Saharan Africa, including Zambia.

Haemoglobin S combined with another abnormal haemoglobin such as C, D, thalassaemia comprises the milder types of SCD. Haemoglobin S combined with normal haemoglobin (HbA), is known as sickle cell trait (SCT), HbAS and is asymptomatic.

The RBCs containing this defective haemoglobin assume a Sickle shape upon oxygen deprivation hence its name Sickle Cell Anaemia. Most sickled cells cannot pass through small blood vessels and blockage of these blood vessels arises. In addition, these sickled cells are easily destroyed leading to chronic haemolysis and anaemia. Most of the symptoms of SCA are as a result of the pathophysiology described above.

Figure 3. 1. Inheritance of Sickle Cell Disease



Medical-dictionary.thefreedictionary.com

This disease is characterized by low haemoglobin levels, bone and joint pain, sometimes with swelling, yellow eyes and recurrent abdominal pain. The cure is very expensive and not accessible to most patients; thus, treatment is directed towards alleviating pain, managing the low haemoglobin by blood transfusion and prevention of infections which are common in sickle cell disease. The disease can be detected in the new-born and older children by examining the blood with special tests.

Reference

1) **The management of Sickle cell Disease.** *NIH Division of blood diseases and resources*. 2014

CHAPTER 4: DIAGNOSIS OF SICKLE CELL DISEASE

To make an accurate diagnosis of any disease condition sickle cell disease inclusive, the standard clinical approach must be followed. This entails collecting a good clinical history, performing a good physical examination, and carrying out appropriate diagnostic tests to confirm the diagnosis. It is therefore imperative that all clinicians understand the clinical presentation of sickle cell disease for early recognition.

Clinical features of sickle cell disease

The time of presentation may vary from one child to another. Most children however begin to manifest symptoms and signs after the age of 3 months when the foetal haemoglobin which is protective begins to diminish. Some children may present even far much earlier or later in life, while some remain asymptomatic. The genotype and variable penetrance of the sickle cell gene contributes to the variability in severity and may have a bearing on the time of presentation. Those who present much earlier in infancy may have more severe disease. Sickle cell anaemia genotype (HbSS) tends to be relatively more severe than the other types of sickle cell disease.

In infancy the early presentations include yellowing of eyes (jaundice), anaemia and dactylitis characterised by painful swelling of hands and feet. Pain may be anywhere, commonly the hands and feet and the abdomen. This is a vaso-occlusive crisis due to blockage of the small blood vessels by the sickled cells. Anaemia is due to haemolysis of the sickled red blood cells whose life span is only 10-40 days as compared to the 120 days of normal RBCs. Sickle cell anaemia patient's normal haemoglobin levels range 6-8g/dl.

Therefore, any child who presents with **recurrent jaundice, recurrent dactylitis** and **abdominal pain** with **anaemia** must be evaluated for sickle cell disease. **Vaso-occlusion** remains by far the commonest cause of hospital attendance; however, few children may present with other crises even for the first time. Infants especially may present for the first time with **splenic sequestration**, characterised by pulling of large volumes of blood in the spleen. The patient presents with hypovolaemia and severe anaemia with a splenomegaly. Other crises are **hyper-haemolytic** and aplastic crisis. Sickle cell patients are always haemolysing, however there are instances that the haemolysis is severe and, in such instances, they present with severe anaemia and deep jaundice. **Aplastic crisis** is triggered by infection with parvovirus B19 which infects and kills off immature RBCs hence resulting in anaemia and a drop in reticulocytes. Children present with severe anaemia with non-corresponding jaundice so as to attribute the anaemia to haemolysis. Sometimes patients may present with a combination of crises. Children with sickle anaemia may also present with several other complications of sickle cell disease, either after diagnosis or first presentation.

Table 4.1: Clinical features of the disease

Infancy	Childhood	Adolescent/Adults
Central Nervous System *Stroke* **Pulmonary System** *Pneumonia* *Tuberculosis* **Musculoskeletal System** *Dactylitis* *Vaso-occlusive crisis* **Gastrointestinal System** *Splenic sequestration* *Jaundice* **Haematological System** *Recurrent anaemia* **Immune System** *Recurrent fevers/infections* *Pneumococcal*	**Central Nervous System** *Meningitis* *Stroke* **Haematological System** *Recurrent anaemia* *Aplastic anaemia* **Urogenital System** *Delayed sexual maturation* *Enuresis* *Priapism* *Urinary tract infection* **Immune System** *Recurrent fevers/infections* *Pneumococcal* *Parvovirus* *Salmonella* **Musculoskeletal System** *Arthritis* *Osteomyelitis* *Vaso-occlusive crisis* **Gastrointestinal System** *Acute abdomen* *Cholecystitis* *Cholelithiasis* *Girdle syndrome* *Hepatitis* **Pulmonary System** *Acute chest syndrome* *Pneumonia* *Tuberculosis* **Cardiovascular** *Cardiomegaly* *Heart failure*	***Haematological System*** *Recurrent anaemia* **Musculoskeletal System** *Avascular necrosis of the femoral head* *Osteomyelitis* *Non-healing ulcer* *Vaso-occlusive crisis* *Arthritis* ***Immune System*** *Recurrent fevers/infection* *Parvovirus* *Salmonella* **Gastrointestinal System** *Acute abdomen* *Cholecystitis* *Cholelithiasis* *Girdle syndrome* *Hepatitis* *Vaso-occlusive crisis* **Urogenital system** *Priapism* *Delayed sexual maturation* *Urinary tract infection* **Pulmonary system** *Acute Chest Syndrome* *Pulmonary hypertension* *Tuberculosis* **Central Nervous System** *Meningitis* *Stroke* **Cardiovascular System** *Cardiomegaly* *Heart failure*

Laboratory Diagnosis of SCD

Screening of SCD in Zambia can be done using the following tests (Fig 4.1):

- Sickle SCAN™ – is a qualitative, point-of-care assay, able to detect haemoglobins A, C and S. This test is available in Zambia and can be used outside the laboratory setting. The test can give an indication to the probable haemoglobin genotype.
- Sickling test – is a laboratory-based assay that screens for RBC sickling. Presence of sickled RBCs indicates that HbS is present in the RBCs. It cannot distinguish between homozygous and heterozygous states.
- Solubility test – is a laboratory-based assay that can distinguish between the relatively insoluble HBS for other haemoglobins. It can distinguish between homozygous and heterozygous states.

Confirmation of SCD and new-born screening for SCD can be done using

- Haemoglobin (Hb) electrophoresis – available in some health facilities.
- Iso-electric Focusing (IEF) – available in limited health facilities
- High performance liquid chromatography (HPLC) – available in limited health facilities

HPLC and some electrophoresis platforms and can quantify the different amounts of haemoglobins while IEF cannot quantify haemoglobin.

Other supporting tests (Which can serve as baseline tests and follow up tests include)

- Complete/Full blood count (CBC/FBC)
- Liver function tests (LFTs)
- Kidney/Renal function tests (RFTs)
- And others as required by patient needs

Documentations of SCD test results

Results of the SCD status should be documented in:

- The patient's medical record
- The patient's electronic data record (e.g. SmartCare)
- The antenatal card
- The under-five card/ART card/TB card
- SCD data registry
- The SCD patient card or any other medical card
- Facility laboratory information system

Linkage to treatment and support services

Linkage to care is a process of actions and activities that support people testing for SCD and those diagnosed with SCD to engage with prevention, treatment, and care services as appropriate for their SCD status. Linkage to care and treatment is the period beginning with SCD diagnosis and ends when a person enters long-term SCD care.

Routine testing for Sickle Cell Disease

Routine testing gives an opportunity to provide immediate treatment and care to all SCD individuals. Health care workers are therefore mandated to offer routine counselling and point of care (POC) SCD testing to all children and pregnant women presenting to health facilities. Screening of adults should be done if they present with anaemia. Routine testing should be offered with the following considerations:

- Provide information on the disease in a confidential manner - those who opt out should continue to be counselled and encouraged to test.
- Provide counselling on benefits of testing and other services available for positive individuals
- Provide accurate results following the correct test procedures
- Provide linkage or connection treatment and care services.

Health care workers are therefore mandated to offer routine counselling and point of care (POC) SCD testing to:

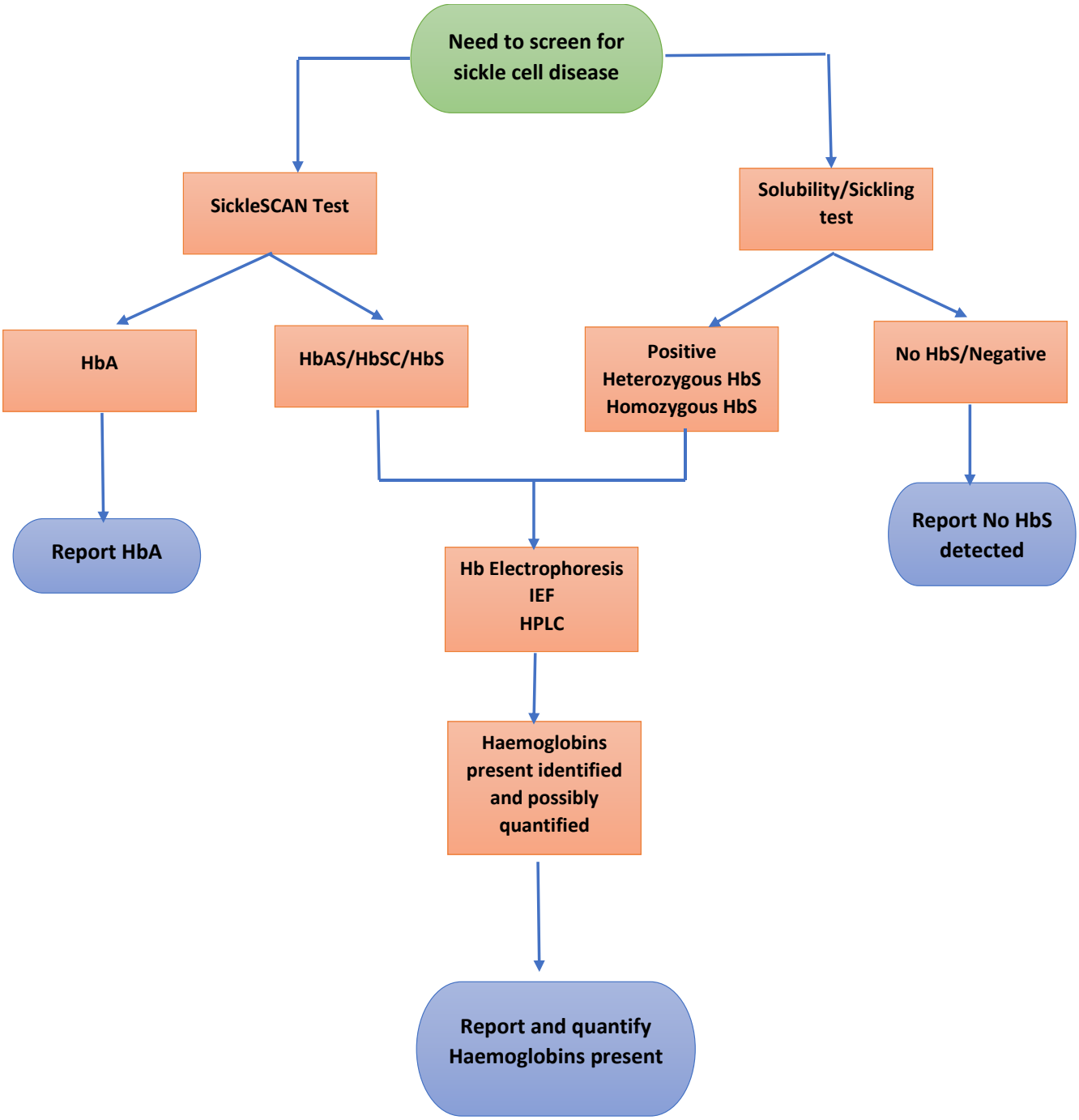
- All children under the age of 5 years (ideally all children)
- Pregnant women during antenatal
- Immediately post-natal if not tested during the antenatal period
- Screening of older children and adults should be done if they present with:
- Bone or/and Joint pains
- Recurrent abdominal pain
- Anaemia
- Jaundice
- Stroke
- Chronic heart, lung, kidney disease
- Cholelithiasis/Cholecystitis
- Avascular necrosis of femoral head (ANFH)

- Osteomyelitis/Arthritis
- Family history of SCD
- Those planning to get married and/or have children

Points of client contact at which testing for SCD can be done include

- Out-patient department
- Emergency department
- In-patient care or In-lay wards
- Under-five clinics
- Antenatal clinics
- Labour/delivery wards
- Post-natal clinics
- HIV testing centres

Figure 4.1: Algorithm for screening and confirmation of SCD in Zambia



New-born screening for SCD

The purpose of new-born screening is to offer the affected child timely and appropriate care such as penicillin prophylaxis, vaccinations including pneumococcal vaccines, as well as teaching the mother to palpate the abdomen daily for sudden enlargement of the spleen or liver.

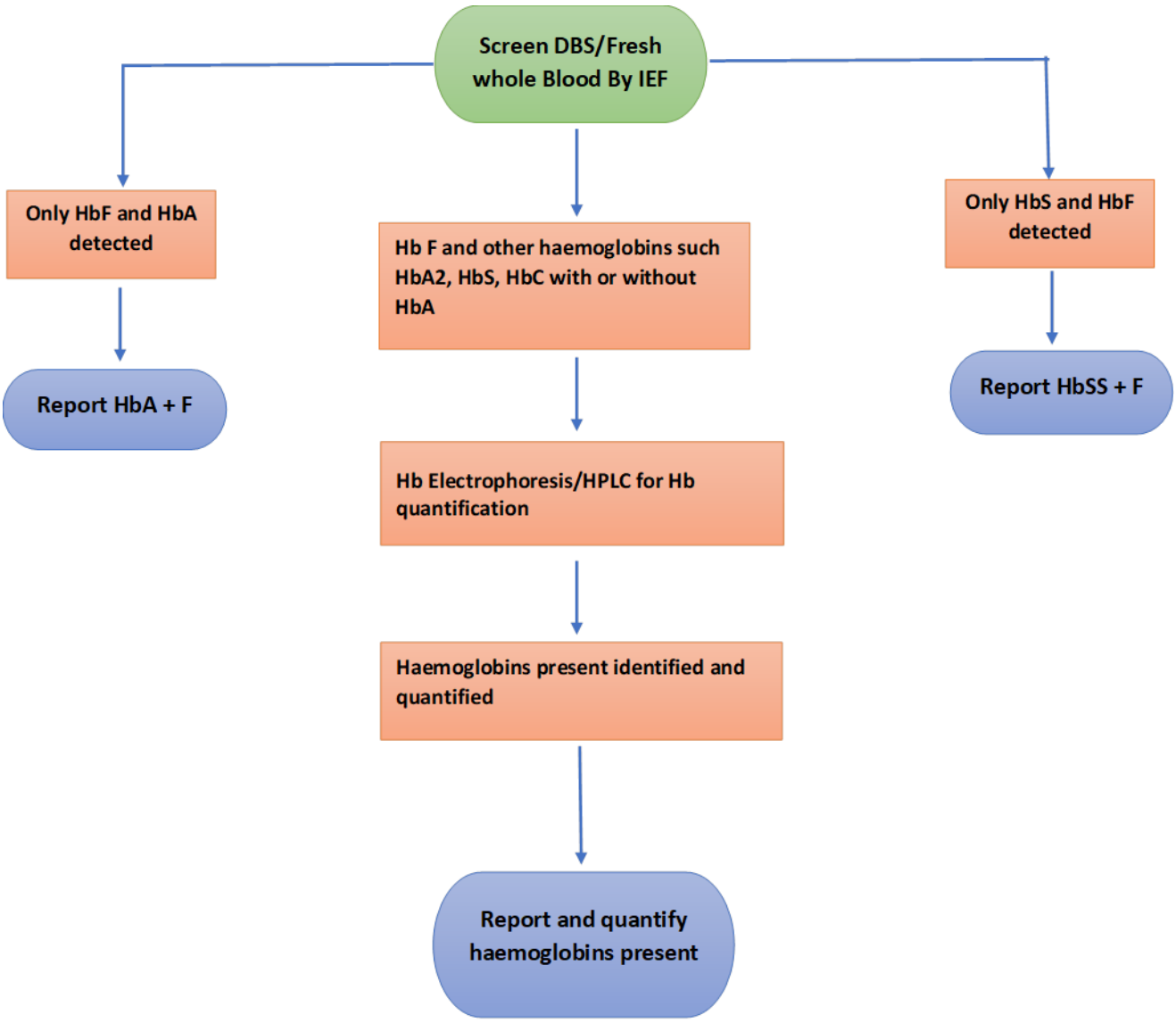
The SCD new-born screening programme is being integrated within the existing health platforms and programmes. In this case screening of children for Sickle cell disease will be conducted as they are being screened for HIV, are accessing under-five vaccinations services or any in or out-patient care services. All children less than 3 months old accessing health services at a health institution will be offered screening for SCD. The rationale behind this strategy is that infants who are first identified as having SCD can be initiated on simple, proven, low cost interventions that have been reported to reduce morbidity and mortality in children with the disease.

Blood for screening of SCD is obtained from the heel of a new-born and spotted on the dry blood spot paper (DBS), which is then tested by either IEF or HPLC (Fig 4.2).

Alternatively, whole blood can be tested using by quantitative haemoglobin electrophoresis.
Results of the test should be communicated to the parent/caregiver during the subsequent growth monitoring or vaccinations visits (Preferably within 4 weeks of testing). Once a positive result is communicated, the newly diagnosed child should be linked to long-term follow up care at your or referral institution.

SCD Registry
Establishment of a SCD registry is important for collecting invaluable information about the condition over time. The registry data can be used to better understand the dynamics SCD in Zambia, provide information that informs health policies for SCD and can also be used for research. It is for this reason that the Ministry of Health supports the development of a SCD registry and encourages all persons with SCD to be registered on the national database.

Fig 4.2: Algorithm for new-born screening for SCD in Zambia



Interpretation of IEF in newborn screening programme

Hb Combinations Identified	Quantities	Interpretation
Hb F Hb A,	Hb F>HbA,	Normal Hb A
Hb F, Hb S,	HbF>HbS,	Sickle cell anaemia*
Hb F, HbS, HbA	HbF>HbA≥HbS	Sickle cell trait
	HbF>HbS>HbA	HbS/ beta^{+} thalassaemia
HbF, HbS, HbC	HbF>HbS>HbC	HbSC disease

* Beta thalassaemia will require HbA2 quantification by the age of 2 yrs to confirm diagnosis. HbA2 >3.6% in beta thalassaemia

Quality assurance/improvement

All samples/patients testing positive for HBS with the screening test should be retested with the confirmatory test. Either the same sample or a fresh sample should be sent to the laboratory for confirmation. If the patient has been previously transfused confirmatory testing should be done at least 3 months after the last transfusion.

All laboratories performing confirmatory testing should participate in external quality assurance programmes.

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CHAPTER 5: OUTPATIENT MANAGEMENT OF SICKLE CELL DISEASE

Monitoring consists of two components: clinical and laboratory

Clinical monitoring includes history, examination, growth and development monitoring in children, as well as evaluation of adherence, side effects, and relevant drug toxicities.

Laboratory tests need to be conducted routinely and as needed

The purpose of monitoring includes:

- Evaluation of treatment response and diagnose treatment failure early
- Evaluation of adherence
- Screening for renal nephropathy
- Detection of toxicity to drugs

When persons with SCD attend outpatient clinic the following need to be done:

a. Change in caregiver and contact details should be updated
b. The patient card should be available and updated
c. Patient should be registered in the national registry
d. Patients/guardians should be asked about any illness in between follow ups and drug compliance should be established, school/work attendance
e. Patients should be evaluated for the current Zambia childhood vaccination schedule including the pneumococcal vaccine.
f. Patients should be examined whether they have complaints or not
g. Weight and height/length to assess the pattern of growth. These parameters are also used to calculate drug dosage.
h. Blood pressure done with appropriate BP Cuff size
i. Pulse oximetry*
j. Urinalysis with a dip stick *
k. Full blood count* Kidney and liver function*
l. The Blood group, HIV and Hepatitis B status should be known
m. Others: iron studies as indicated, Hb electrophoresis at diagnosis and follow up for treatment response
n. Transcranial doppler to children between the ages of 2 and 12 years (refer to CNS)
o. Prophylactic folic acid, anti-malaria and penicillin (erythromycin for penicillin allergic patients) should be prescribed
p. Age appropriate counselling

*** The tests must be done within the same day of review and results should be available within the same day.**

*** Those with abnormal pulse oximetry results should be referred for lung functions tests and ECHO cardiogram**

Table 5.1: Clinical and laboratory monitoring

Age	Clinical visit	Blood workout
0-6 months	Monthly	FBC
6 months- 2 years	Every 3 months	FBC
2 years-5years	Every 6 months	FBC *Yearly Urine LFTs and RFT
Over 5 years	6-12 months	FBC, pulse oximetry *Yearly Urinalysis LFTs and RFT
Adolescents	Yearly	FBC, *Yearly Urine LFTs and RFT, age appropriate counselling
Adults	Yearly	FBC Yearly Urine LFTs and RFT

Growth monitoring

The monitoring of growth and nutritional status in children with SCD is an essential requirement for comprehensive care, facilitating diagnosis of growth failure and nutritional intervention.

It is worth noting that SCD affected children have normal weight and length at birth, and then at about 6 months of age, their growth patterns start to diverge from the norms for age due to the advent of the first clinical events of the condition

Later in life, height and weight for most of them would be significantly lower when compared with their unaffected counterparts.

Delayed pubertal development occurs as a result of endocrine and metabolic dysfunction associated with the course of the condition.

This calls for an early growth monitoring schedule as part of comprehensive care for children with SCD. Besides regular haematologic assessment, height, weight and motor milestones should be recorded at every visit in order to implement timely corrective measures

References

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2) Platt OS, Brambilla DJ, Rosse WF et al. **Mortality in sickle cell disease. Life expectancy and risk factors for early death.** *N Engl J Med.* 1994;330(23):1639–44.

CHAPTER 6: MANAGEMENT OF SPECIFIC CONDITIONS

1. Painful crisis

Pain is a common, underreported and underdiagnosed problem for hospitalised children worldwide including sickle cell patients. Unrecognized pain is worse for infants and mentally challenged children. In the sickle cell patient, vaso-occlusive pain due to occlusion of blood vessels by sickled cells commonly presents with painful hands and feet in the young child and pain in the long bones in the older children. Abdominal pain due to occlusion of the mesenteric blood vessels is also a fairly common occurrence and may mimic an acute abdomen. These painful episodes may however occur anywhere in the body (Table 6.1).

Table 6.1 Pain Syndromes in Sickle Cell Disease

Acute pain syndromes	Chronic pain syndromes
Vaso-occlusive crisis	Avascular (aseptic) necrosis
Hand-foot syndrome	Arthritis
Acute chest syndrome	Leg ulcers
Cholecystitis/Cholelithiasis	Vertebral body collapse
Priapism	Arthropathy
Splenic sequestration	

In the sickle cell patient presenting with pain, the following steps must be taken

Step I:

Establish Intravenous (IV) access.

Begin with hydration to facilitate circulation of blood: use 5% Dextrose normal saline IVF (1.5 x maintenance or 2,250 ml/ square metre/day) if no cardiopulmonary compromise.

Step II:

Assess for cause and severity of pain and complications. Use pain assessment tool (See appendix). Ask the patient to rate the pain as mild/moderate/severe. Ask about site, severity and duration of pain (usually bones/spine/abdomen). Conduct a complete systemic examination to look for complications.

Step III:

- Give analgesia as per guidelines (Table 6.2)
- If febrile, commence IV antibiotics
- Monitor pulse, respiratory rate and oxygen saturations
- Look out for side effects of morphine- nausea/vomiting, pruritis, drowsiness and constipation. Always prescribe laxatives (stool softener + stimulant) when starting opioids.

Step IV

- Stop IV fluids when the patient is stable, and pain controlled
- Weigh the child daily
- Avoid fluid overload

Pain Management

- **Assess the intensity of the pain by using**: “face pain” intensity scale or visual analog scale (See appendix 1), multi- dimensional scale, clinical acumen.
- **Use WHO analgesic ladder which advocates for a stepwise approach to treating pain depending on the severity of the pain** (Table 6.2)**.** At every step of the analgesic ladder, non-opioid analgesics

form the basis of the pain management. Paracetamol and NSAIDs (if not contraindicated) should always therefore be prescribed with opioid analgesia.

- **Treat pain aggressively and promptly**. Begin analgesic management within 15 minutes of triage or within 30 minutes of registration.

Table 6.2: WHO stepwise approach to pain management

Severity	**Management**
Mild	Reassurance, warm packs, reposition, massage, distraction (stories, play) **Child:** Paracetamol 15mg/kg QID **Adult**: Paracetamol 1g QID
Moderate	As for mild pain, PLUS **Child**: Ibuprofen 5mg/kg TDS OR Diclofenac 1mg/kg TDS **Adult**: Ibuprofen 400mg TDS OR Diclofenac 100mg TDS
Severe	As for moderate pain PLUS **Child**: Oral morphine 0.2- 0.3mg/kg 4 hourly as needed **Adult**: Oral morphine 5- 10mg 4 hourly as needed

Administration of Morphine

Morphine is a pain medication of the opiate family. Opioids occur naturally in a number of plants, animals as well as human beings. Endorphins are naturally occurring opioids in the human body. When released, endorphins interact with receptors in the brain and reduce perception of pain as well as trigger a positive feeling in the body. The opiate morphine is derived from the poppy plant and has the same action in the body as endorphins.

Oral Morphine

Morphine given as Morphine sulphate solution or tablet is indicated for moderate to severe morphine responsive pain. It has a biological half-life of 3-4 hours necessitating the 4-hourly dosing.

Commencement of treatment

- Morphine starting dose for patients <50kg including children is 0.15-0.3 mg/kg given 4hourly.
- Morphine starting dose for patients >50kg is 5-10 mg given 4 hourly.
- The starting doses must be strictly adhered to as a high starting dose causes respiratory depression and drowsiness.
- The weight appropriate starting dose must be given every 4 hours, 4 times during the daytime.
- The night dose is given as a one and a half (1.5x) to double (2x) single daytime dose to allow undisturbed sleep.

Follow-up treatment

- After starting treatment review effect after 1-2 hours. If little or no effect Increase dose by 50%.
- Review again after 12-24 hr. If breakthrough pain is occurring at 2-3 hours before the 4-hour half-life of the drug, increase dosing by 50%.

- If still in pain: review dose, review cause, ask 'is this morphine responsive?', add, or replace with, adjuvant drugs.

Morphine dosing is individually determined depending on the pain response. There is no upper limit to dose as long as dosing increased systematically and slowly according to pain response. As much as possible the initial dose should be anchored to waking up time of the patient.

Morphine - Intravenous and Subcutaneous Dosing

Morphine is ideally given by mouth and should be given orally unless it is not possible to give it orally.

If it must be given as intravenous (IV) infusion or subcutaneously (SC), **parenteral dose should be 1/3 (one third) of oral dose.**

Dosing

- In children, **0.03mg/hour if continuous infusion, or 0.05-0.1mg/kg every 2-4 hr subcutaneous.**
- In Adults, **add up total oral dose in 24 hr, divide by 3 and set rate to deliver over 24hrs.**

e.g. starting dose is 5mg per dose, total 24 hr dose is 5x4= 20mg +1.5x night time dose 7.5mg. Total oral 24 hr dose =20+ 7.5mg =27.5mg. Parenteral dose =27.5/3=9.1mg (rounded off as 9mg. Deliver this over 24 hrs.

Side effects

- Nausea and vomiting – wear off after 3-5 days, give anti-emetic if nausea occurs.
- Constipation – occurs in 100% of patients -always give laxative (e.g. lactulose) with stimulant and softening effects; advise about increasing liquid intake and high fibre foods.
- Drowsiness – wears off after 3-5 days; reduce dose and titrate more slowly.
- Hallucinations and myoclonic jerks – occur in 2% or so; reduce dose or stop drug.
- Respiratory depression – occurs only in overdose e.g. if drug dose has been increased too quickly – check for pin-point pupils, respiratory rate, give **IV naloxone slowly (this is an antidote for Morphine over-dosing).**

Naloxone Dosing for morphine overdose

- **Neonates:** 0.01-0.1 mg/kg IV
- **Children :**0.01-0.1mg/Kg IV
- **Adults:** 0.4 mg to 2 mg IV; doses can be repeated at 2 to 3-minute intervals up to total dose of 10 mg if no response is observed with initial dosing.

Stoppage of treatment

If morphine has been administered for more than a week doses must be tapered down slowly to avoid withdrawal symptoms.

Reference

1) **Update: WHO revision of pain management guidelines**
2) https://www.who.int/maternal_child_adolescent/guidelines/scope-guideline-pain-in-children.pdf
3) World Health Organization, (2009). **WHO's Pain Relief Ladder**. www.who.int/cancer/palliative/painladder/en/
4) SWRWC Toolkit_B.5.3 **WHO Pain Ladder with Pain Management Guidelines** _Jan 7_2011 Adapted from a CarePartners/ ET NOW form with permission 2010.

2. Acute anaemia in SCA

Acute anaemia in SCA is a precipitous fall of haemoglobin concentration by 2.0g/dL or more below an individual's steady state (baseline) Hb concentration. Generally, in SCA patients (HbSS) the Hb baseline levels are between 6-8g/dL)

Differential diagnosis

A. Acute splenic sequestration crisis
B. Aplastic crisis
C. Hyper- haemolytic crisis

A. Acute splenic sequestration crisis and Hypersplenism

Acute splenic sequestration is an **EMERGENCY** condition where there is sudden pooling of blood mostly in the spleen but can sometimes also occur in the liver. This can lead to severe anaemia, shock and if it is not attended to quickly, death.

On examination of the affected child, there is pallor, tachycardia, signs of hypovolaemic shock and an enlarged tender spleen. This condition affects children usually up to the age of 3 years, with a peak at 1 year of age.

Investigations

- Full blood count- severe anaemia
- Reticulocyte count (Elevated reticulocyte count = Splenic sequestration crisis/ Hypersplenism)

Management:

Management of **acute sequestration** consists of management of shock and blood transfusion.

- The immediate definitive management is urgent transfusion of 20ml/kg of whole blood.
- If blood is not available, 20ml/kg of normal saline should be given over 30 minutes and patient should be evacuated to a higher centre that is able to give blood transfusion.
    - During the transfer, the normal saline can be repeated if the patient's vitals are not stabilised (Appendix 3)

Hypersplenism is a chronic enlargement of non-tender spleen associated with pancytopenia. Children affected are usually above the age of 3 years.

Both conditions require splenectomy to be done. For Acute splenic sequestration, splenectomy should be done as soon as the patient is stabilised.

Post-splenectomy complications:

Rebound thrombocytosis after splenectomy occurs immediately after surgery and should be monitored closely.

B. Aplastic crises (Transient red cell aplasia [TRCA])

Aplastic crisis is severe anaemia developing secondary to temporary suppression of erythropoiesis. Most (70-100%) cases of TRCA are due to human parvovirus B19 infection. Parvovirus B19 directly infects erythroid precursors and destroys them.

****It is unusual for one to have a subsequent aplastic crisis due to parvovirus B19 as immunity developed from initial parvovirus infection is lifelong. Thus, other causes of red cell aplasia must be sought for if one presents with a second episode aplastic crisis****

Investigations

- FBC – severe anaemia,
- Reticulocyte count (Depressed reticulocyte count-reticulocytopenia)
- Parvovirus B19 IgM – Positive

Management

- Packed red cell transfusion to correct anaemia
- Monitoring of reticulocyte count to monitor recovery

Complications of TRCA

- Bone marrow necrosis
- Stroke
- Acute chest syndrome
- Glomerulonephritis
- Sequestration

C. Hyper- haemolytic crisis

Severe anaemia developing secondary to massive intravascular haemolysis. The hyper- haemolytic crisis may occur concomitantly with VOC. Patient may present with sudden onset development of or worsening of already existing jaundice.

Most common precipitating factors include

- Infections including malaria
- Drugs

Investigations

- Investigate for possible precipitating factor including infections

- FBC– anaemia
- Reticulocyte count (Elevated reticulocyte count- reticulocytosis)
- Lactate Dehydrogenase (LDH) – Greatly elevated
- Bilirubin – Indirect bilirubin greatly elevated
- Direct Antiglobulin Test (DAT) – should be negative (If positive investigate for autoimmune haemolytic anaemia

Management

- Transfusion may be required to correct anaemia
- Treat any underlying infection
- Withdrawal possible or identified offending agents, such as drugs

Reference

1) **The management of Sickle cell Disease.** *NIH Division of blood diseases and resources.* 2014.

3. Infections

Infections are a major complication of SCD. **Infections, especially pneumococcal septicaemia, meningitis, pneumonia, and *Salmonella* osteomyelitis are a major cause of morbidity and mortality in patients with SCD.** A 20-years prospective study showed for instance that bacterial infections (Bis) led to 20–50% of deaths among SCD patients. The increased susceptibility of SCD patients to BIs is multi- factorial, including: (i) a functional asplenia; (ii) a default in complement activation; (iii) micronutrient deficiencies; (iv) a genetic predisposition, and (v) mechanical risk factors. Most infections are treatable

Clinical features of infection in SCD

- Fever is a common sign of infection
- Fever may be associated with other signs and symptoms such as:
- Bone tenderness
- Difficulties in breathing and chest pain
- Diarrhoea, vomiting
- Jaundice
- Stiffness of the neck and headache
- Lymphadenopathy
- Fever may not be present in some patients with an infection
- Patient may have other signs such as pallor and dehydration

Investigations:

- Record temperature, (axillary if above 2 years and rectal if below 2 years
- Blood pressure
- Full blood count
- Malaria parasite slide or RDT
- Urinalysis – Routine microscopic culture and sensitivity
- Blood culture
- Respiratory rate
- Collect Sputum for culture and sensitivity
- Chest X-ray
- Sputum for TB should be collected
- Lumbar puncture if indicated
- Nasopharyngeal aspirate for PCP or gastric aspirate
- Blood culture

Empirical Treatment

- Hydration
- Oxygen if indicated
- Blood transfusion if HB is less than 5g/dl
- Paracetamol
- Children with temperature of 40ºC and above should be admitted to hospital and should receive parenteral antibiotics
- Children with temperature of less than 38ºC should be observed before being sent on house therapy
- Antibiotics – Penicillin, crystalline or procaine, chloramphenicol or cefotaxime alone. The antibiotics should be changed to oral when the child's condition has stabilised
- Antibiotics should be given for at least 7 days
- If a child is not responding to antibiotics within 48 hours and blood and sputum cultures are negative, and they have signs and symptoms of pneumonia, think of other causes of pneumonia such as pulmonary tuberculosis, PCP, mycoplasma pneumonia

Specific Treatment

Treatment should be as per guidelines for the specific diagnosis

References

1) Booth C, Inusa B, Obaro SK. **Infection in sickle cell disease: a review.** *Int J Infect Dis.* 2010;14(1): e2–e12.
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3) Alima Yanda et al. **Burden and spectrum of bacterial infections among sickle cell disease children living in Cameroon.** *BMC Infectious Diseases* (2017) 17:211
4) Cannas G., Merazga S., Virot E. **Sickle cell disease and infections in high- and low-income countries.** *Mediterr J Hematol Infect Dis* 2019, 11(1

4. Priapism

Definition

Priapism is a sustained, unwanted painful erection, unrelated to sexual stimulation and unrelieved by ejaculation. Priapism is a common complication. About 80% of boys and men with SCA will have experienced at least one episode of priapism by the age of 20 years. Prompt recognition of priapism and immediate initiation of conservative medical management may lead to detumescence (penis returning to flaccid state) and limit the need for more aggressive and invasive intervention.

Classification

1. Prolonged – Penile erection lasting more than 4 hours is an EMERGENCY CONDITION
2. Stuttering – Repeated penile erections lasting more than a few minutes but less than 4 hours. Stuttering priapism will usually resolve spontaneously but may recur and may develop into prolonged events.

Evaluation of patient with priapism

- Document time of onset of erection
- Document possible inducing factors
    - Trauma
    - Infection
    - Full bladder
    - Prolonged sexual activity
    - Drugs
    - Alcohol
    - Psychotropic agents
    - Sildenafil (Viagra)
    - Testosterone
- Examination will reveal hard penis with soft glans

Management

1. **At onset of priapism**

    - Oral fluids
    - Patient to be advised to attempt urination
    - Oral analgesics
    - Walking may be helpful and warm baths may also help avert early priapism, by improving blood circulation

2. **Penile erection lasting more than 4 hours**
    - Intravenous rehydration 2,000mL/m²/day (1.25 x maintenance) if there is no cardiopulmonary compromise.
    - Pain control with opioid analgesics
    - Anxiolytics
    - Institute a simple pRBSC transfusion 10ml - 15ml/kg
    - Consult urology immediately for aspiration and irrigation
    -

3. **If detumescence (flaccidity) not achieved within 1 hour of admission at emergency room**
    - Institute penile aspiration and corporal irrigation (Penile aspiration to be instituted within 4-6 hours from onset of priapism)
    - Prepare a 1:1,000,000 solution of epinephrine in saline
    - Sedate patient and administer local anaesthesia
    - Aspirate blood from corpus cavernosum using a 23-gauge needle until detumescence.

- Irrigate corpora with epinephrine solution (add 1ml of 1% epinephrine to 39ml normal saline to make 0.25mg epinephrine and inject 1ml directly into the corpus cavernosum with a 27-gauge needle). The injection can be repeated every 15 minutes up to a maximum of 6 injections.

4. **Surgical shunts:** if the above measures fail to relieve priapism, a shunting procedure will be necessary.

General SCD care and counselling of patients on effects of priapism i.e. impotence and possibility of recurrence should be mentioned to the patients after recovery from the episode.

Complications

Complications usually arise from frequent and recurrent episodes of priapism

- Fibrosis
- Impotence

Reference

1) Mantadakis E; Cavender JD; Roger ZR. **Prevalence of priapism in children and adolescents with sickle cell anaemia.** 1999 21; 518-522.

5. Thrombocytosis in sickle cell anaemia

Definition

A benign condition characterised by a reactive (secondary) increase in the number of platelets of ≥ 450 × 10^9/L due to various stimuli.

Differentials

- Clonal (essential) thrombocytosis,
- Chronic Lymphocytic Leukaemia,
- Chronic Myelogenous Leukaemia,
- Polycythaemia Vera and
- Thrombotic Thrombocytopenic Purpura.

Investigations

Should be guided by what we find from the history and physical examination.

Laboratory investigations

- FBC
- Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP)
- Malaria parasite slide (MPS)
- Peripheral blood smear (PBS)
- LFT's
- U&E's
- Iron Studies
- Antinuclear antibody (ANA)
- Rheumatoid factor (RF)
- Cytogenetic Analysis
- Bone marrow aspiration
- Biopsy

Imaging studies

- Abdominal ultrasound scan.

Management

- Treatment of the identified cause.
- For platelets ≥ 1000 × 10^9/L, antiplatelet agents e.g. Low- dose aspirin should be considered.

Complications

- Thrombo-embolic episodes e.g. stroke

References

1) Chiarello P, Magnolia M, Rubino et al. **Thrombocytosis in children.** *MinervaPediatrics*. 2011.
2) Kumar P, Clark M. *Clinical Medicine*. 8th edition. 2012. Saunders Ltd.
3) *www.emedicine.com/thrombocytosis*

6. Acute chest syndrome (ACS)

A clinical condition which mimics a severe pneumonia in a SCA patient. It is the second most frequent reason for hospitalisation in children and adults with SCA and the most common cause of death. It can develop suddenly or insidiously during hospitalisation for a VOC or after a surgical procedure.

A person with ACS typically has sudden onset of signs and symptoms of lower respiratory tract disease [e.g., cough, shortness of breath, nasal flaring, chest pain, hypoxia (<95% on room air), retractions, etc.] The most common well-defined aetiology is infection (e.g., viral, bacterial. chlamydia, or *Mycoplasma*), but the complication may also result from bone marrow fat embolism, intrapulmonary aggregates of sickled cells, atelectasis, or pulmonary oedema.

Risk factors

- Young age
- Low foetal Haemoglobin (HbF)
- High steady state Hb
- High Steady state WBC
- >3 episodes of VOC in the preceding year
- Asthma/airway hyperactivity
- Tobacco smoke or exposure
- Recent surgery

Differential diagnosis

- Severe pneumonia
- Severe malaria with severe anaemia
- Asthmatic attack
- Pulmonary tuberculosis (PTB) – investigate those with recurrent pneumonia or ACS
- Bronchiolitis
- Laryngo-tracheo-bronchitis (LTB)
- Foreign body

Investigations

- FBC with differential count
- Reticulocyte count
- Group and X-match
- Blood culture
- Total bilirubin
- LDH
- Chest X-ray (CXR) - PA and lateral view (NOTE: 60% of children with acute chest syndrome will have an infiltrate on CXR but a normal pulmonary exam).
- CRP/ESR
- U&Es
- LFTs
- Pulse oximetry

Management

- Hydration: Intravenous fluids (IVF) at 2/3 maintenance, maximum, depending on oral intake. Can decrease or discontinue IVF if taking enough per oral (PO) fluids to meet daily maintenance goal, (1,600mL/m^2/day). Over-hydration can lead to pulmonary oedema and worsen the acute chest syndrome.
- Continuous monitoring of the pulse, respiratory rate, oxygen saturations and blood pressure.
- Pain management: Be cautions with narcotics but do not withhold. Balance between pain control and sedation as either may lead to respiratory distress. Narcotics can lead to hypoventilation and worsen acute chest syndrome *(refer to section on pain management)*
- Respiratory care: Oxygen therapy with pulse oximetry monitoring. Maintain oxygen saturation at >94%
- Blood transfusion indications: Institute a simple pRBC transfusion at 10 - 15mL/kg, if:

        - Severe anaemia (Hb <7g/dL or if Hb drops <2 g/dL from baseline)
        - Significant hypoxia, or
        - Worsening respiratory status.
- Antibiotics for pneumonia: Cefotaxime 200mg/kg 8 hourly IV + Erythromycin 10mg/kg in 4 divided doses PO for 10 -14 days
- Bronchodilators: To be given if there is presence of wheeze of history of reactive airway disease

Complications

Recurrent episodes of ACS can lead to:

- Chronic hypoxaemia
- Atelectasis
- Obstructive pulmonary disease
- Restrictive lung disease
- Fibrosis
- Cor pulmonale
- Pulmonary Hypertension

References

1) Jain S, Bakshi N and Krishnamurti L**. Acute Chest Syndrome in children.** *Pediatr Allergy Immunol Pulmonol. 2017 Dec 1:30(4):* 191-201

2) Vichinsky EP et al. **Causes and outcomes of the acute chest syndrome in sickle cell disease.** *National Acute Chest Syndrome Study Group. N. Engl J Med* 2000:342:1855-1865

7. Renal disease in SCA

The renal manifestations of SCA are diverse and account for 16-18 % of overall mortality in this patient population. The pathogenesis is complex but is associated with hypo-perfusion in selected areas of the kidney such as the medulla, whole kidney hyper-perfusion and ischemia –reperfusion injury.

The inner medulla's relatively hypoxic, hypertonic, and acidotic environment is known to predispose to sickling of RBCs, which significantly decreases renal medullary blood flow through vaso-occlusion. This leads to repeated occlusion that may result into papillary necrosis, haematuria and deranged tubular function. Proximal tubule dysfunction generally impairs urinary concentration, while more distal tubule dysfunction may impair potassium excretion, leading to hyperkalaemia (as seen in various forms of renal tubular acidosis). Paradoxically there is also concomitant whole kidney hyper-filtration which results in glomerular hypertrophy and works in concert with the other mechanisms to result into progressive kidney disease associated with an eventual reduction in glomerular filtration rate.

Renal manifestations of SCA can occur at any age and are more likely to do so in homozygous disease. Kidney hypertrophy, hyperfiltration and impaired urinary concentrating ability have been reported in infancy. Haematuria and AKI can occur at any age whereas microalbuminuria and reduced glomerular rate are prone to occur in early to middle adulthood.

Potential renal manifestations of SCA

- Altered haemodynamics (hyperfiltration, supra-normal GFR, decreased medullary perfusion)
- Gross haematuria
- Reduced ability to concentrate urine
- Distal nephron dysfunction
- Glomerulopathies (FSGS)
- Proteinuria
- Acute kidney injury
- Chronic kidney disease (reduced GFR)
- Increased risk of urinary tract infections
- Renal medullary carcinoma (more common in sickle cell trait)

Investigations

The diagnosis of sickle cell nephropathy is based on the clinical signs and symptoms of the condition, as well as on laboratory and imaging test results. Before concluding that observed renal derangements are primarily secondary to SCA, other aetiologies must be ruled out. This is done by conducting the usual investigations recommended for the particular renal manifestation. In patients with possible sickle cell nephropathy, the following tests are recommended:

Laboratory studies

- Urinalysis looking for haematuria and proteinuria
- Urine microscopic analysis
- Renal Function tests
- Hepatitis B and C virus (HBV and HCV) and human immunodeficiency virus (HIV) tests administered because of the increased risk of transfusion-related infectious diseases in patients with sickle cell disease, who may require multiple blood transfusions.

Imaging studies

- Ultrasonography can be used to exclude other causes of post-renal or obstructive uropathy (e.g., nephrolithiasis),

- Intravenous Pyelogram (IVP) which will evaluate the excretory function of the different parts of the kidney
- CT Scan with and without contrast to exclude renal medullary carcinoma in patients presenting with haematuria.

Gross Haematuria

SCA associated gross haematuria is usually painless and can occur at any age. In SCA, treatment of gross haematuria consists of bed rest and maintenance of high urine flow rate by increasing fluid intake and maintaining the urine output at more than 1ml/kg/min while ensuring hemodynamic stability (monitor BP, pulse rate, peripheral perfusion). Lasix may also be used additionally to induce a diuresis. In cases of massive haematuria, one should consider iron replacement and/or blood transfusions. In the majority of cases, however, haematuria is self-limited. Further investigation by way of ultrasound in the case of persistence of gross haematuria is required so as to ensure that entities such as renal tumours and stones are detected. In such cases patients should be referred for further evaluation.

Proteinuria

Is more likely to occur after adolescence. Usual baseline investigations for persistent proteinuria such as serum albumin, serum lipid profile, infectious and immune panels should be done to rule out other aetiologies. Early nephrology consultation is advisable.

Although no specific treatment slows or prevents the progression of sickle cell nephropathy to end-stage renal disease (ESRD), evidence suggests that the reduction of proteinuria may be beneficial. The use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) has been shown to reduce proteinuria and to be particularly reno protective. This effect is perhaps explained by the ability of these compounds to lower intraglomerular pressure. ACE inhibitors are recommended even in the absence of hypertension for the reduction of persistent significant proteinuria.

Hypertension in SCD associated nephropathy

ACE inhibitors are the drug of choice for treating hypertension secondary to SCA nephropathy. Care must be taken to monitor for potential side effects of hyperkalaemia and reduction of the glomerular filtration rate particularly with more advanced stages of chronic kidney disease.

Anaemia in SCA with CKD

Anaemia in patients with SCA with chronic kidney disease is managed differently from anaemia due to chronic kidney disease secondary to other causes. The recommended goal is for a haemoglobin concentration of no greater than 10g/dL or a haematocrit of no greater than 30%, because red blood cell (RBC) sickling (VOC) is more likely to occur with higher haemoglobin levels. A rise in the haematocrit of greater than 1-2% per week should be avoided.

Erythrocyte-stimulating agents, such as erythropoietin can be used to achieve the appropriate haemoglobin concentration.

For patients presenting with severe anaemia not related to chronic renal disease refer to the sections on management of acute and chronic anaemias.

End-Stage Renal Disease (ESRD)

All forms of dialysis are acceptable in patients with sickle cell disease and choice of exact modality being dependant on the usual considerations. Renal transplantation is possible though outcomes are not as good as patients without SCA. Recurrence of sickle cell nephropathy in the transplant kidney is also a possibility

References

1) PlattOS, et al. **Mortality in sickle cell disease. Life expectancy and risk factors for early death.** *N. Engl.J. Med* 1994;330:1639-1644

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8. Central nervous system (CNS) manifestations of SCA

A. Stroke

Stroke, defined as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, of vascular origin, is one of the major complications of SCD, with the homozygous S disease (HbSS) type having the highest risk. Stroke in SCA affects the large vessels of the arterial circulation of the brain. There is progressive occlusion of these arteries by fibrin proliferation and thrombi leading to endoluminal narrowing. This causes fast and turbulent blood flow within the vessels, measurable by Transcranial Doppler (TCD) ultrasound waves. SCA cerebral vasculopathy can cause both overt stroke and silent cerebral infarcts. Brain dysfunction occurs when oxygen supply to the brain falls below a critical level based on need. Stroke in children can be either ischaemic (usual) or haemorrhagic.

Common clinical features

- Hemiparesis,
- facial weakness
- Severe headache (w/without associated vomiting)
- Visual and language disturbances
- Seizures (especially focal seizures)
- Altered sensation, behaviour and mental status
- Coma.

Differentials

- CNS infections (Meningitis/Encephalitis)
- Cerebral malaria
- Trauma with consequent subdural hematoma
- Intoxication, particularly if focal signs are not prominent.

Investigations

- Malaria parasite slide,
- Full septic workup
- Full blood count
- Renal and liver functions tests
- Cross- match
- Neuroimaging if available, urgent non-contrast CT (to look for haemorrhage/ infarct)/ MRI (if infarct present, perform MRA and MRV)
- Where available an Electro-encephalogram (EEG) can be done

Prevention of stroke

Primary Stroke prevention: SCD children with abnormal transcranial doppler measurements (mean maximum velocities of greater than 200cm/s) in the distal portion of the internal carotid and proximal portion of the middle cerebral arteries should be offered chronic transfusion therapy to reduce HBs levels to below 30% and subsequently switched to Hydroxyurea (exclude severe MRA-confirmed vasculopathy). If blood transfusion is not feasible, Hydroxyurea (20mg/kg/day or maximum tolerated dose) can be used.

Investigation and Interventions:

Transcranial doppler (TCD) ultrasound identifies children with SCD at risk of stroke, allowing preventive interventions. Usually performed in children from the ages of 2-16 years.

- Abnormal TCD: >200cm/sec: Chronic blood transfusion. Repeat TCD at 6 months

- Conditional TCD: 170 – 199cm/sec: Repeat TCD in 1-3 months
- Normal TCD: <170cm/sec: Repeat TCD yearly.

Secondary stroke prevention: Chromic blood transfusion/ hyper-transfusion therapy is the preferred over hydroxyurea for secondary stroke prevention. Look out for iron overload. Hydroxyurea can be given if blood transfusion is not feasible.

Management

The approach to management depends on specific type of stroke (Ischaemic vs haemorrhagic).

Ischaemic stroke

- Stabilise (airway, breathing, circulation) and admit patient to intensive care unit
- Supportive care measures- maintain normothermia, normoglycemia, NPO, correct hypoxia and systemic hypotension
- Keep the head flat (unless high suspicion for raised intracranial pressure)
- Adequate hydration with isotonic fluid at least two third of requirements to guard against cerebral oedema.
- Seizures should be controlled with appropriate antiepileptic drugs *(*see appendix 5 for management of status epilepticus). There is no indication for prophylactic antiepileptic medication.
- Immediate simple blood transfusion with packed cells or exchange transfusion within four- six hours of admission. This should be followed by hyper transfusion protocol (*see appendix 2).* HB after initial transfusion should be maintained around (but not greater than) 11g/dl to avoid development of hyper viscosity syndrome.
- Regular (2-4 hourly) Glasgow Coma Scale and vitals (pulse rate, blood pressure and respirations) monitoring to look out for Cushing triad of raised intracranial pressure.
- Commence hydroxyurea at 20-25mg/kg/day *(refer to sections on essential drugs)*
- Empirical antibiotics if fever is present and high suspicion of infection.

Haemorrhagic stroke

Adults are more affected by haemorrhagic strokes than children. Despite being rare in children, haemorrhagic stroke is associated with high mortality rates.

Common clinical features

- Severe headache,
- Vomiting
- Coma.

Risk factors for haemorrhagic stroke in children

- Low steady state haemoglobin count
- High leucocyte count.

Information on management of intracerebral haemorrhage in SCD is scarce. Simple blood transfusion can be considered though its efficacy has not been proven except in patient with both ischaemic and haemorrhagic strokes.

- Admit to the intensive care unit
- Stabilize the patient- airway, breathing, circulation
- Manage hyperthermia, hypoglycaemia, hypotension
- Manage raised intracranial pressure if present
- Correct thrombocytopenia and coagulation abnormalities

- Consult neurosurgeons- VPS indicated for obstructive hydrocephalous

References

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B. Seizures

A seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain that may be manifested as involuntary motor movements and/ or non-motor episodes (i.e. blank stares, automatisms, hallucinations and personality and behavioural changes) alone or in any combination. Focal seizures may manifest with or without loss of awareness.

Differentials

Seizures in SCA patient may indicate:

- Stroke
- CNS Infections
- Malaria
- Febrile convulsion
- Metabolic derangements like hypoglycaemia and electrolyte imbalance.

Investigations

- Full blood count and differential count
- Renal and Liver function tests
- Electrolytes
- Blood cultures
- Random blood sugars
- Cross match
- Malaria Parasite Slide / RDT for malaria
- Lumber puncture (if not contraindicated)
- EEG, if available
- Neuroimaging, urgent non contrast brain CT/MRI to rule out infarcts/ haemorrhage
- Toxicology screen, if indicated

Management

- Stabilize the patient- secure airway, breathing circulation
- Evaluate and treat appropriately the cause of the seizure
- Correct hypoxia
- Correct hypoglycaemia
- Institute appropriate antiseizure therapy for adults and children presenting in status epilepticus *(see appendix 5)*
- Anti-pyretic such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAID) such as Ibuprofen, diclofenac
- Antibiotics as per treatment guideline for meningitis and/or anti-malarial as per treatment guideline for malaria
- Correct underlying electrolyte derangements
- Initiate long term antiepileptic therapy if indicated (*see appendix 4 for proposed choice of drugs)*

Reference

1) Farooq S, Testai FD. **Neurologic Complications of Sickle Cell Disease**. *Curr Neurol Neurosci Rep* 2019; 19: 17.

C. Central Nervous System (CNS) infections

Infection is a major complication of SCA. CNS infections are not uncommon, inclusive of bacterial, viral or parasitic and are a high cause of mortality. Infections of the CNS in children with SCD may predispose them to stroke.

Clinical features

- Headache
- Vomiting
- Neck stiffness
- Photophobia
- Fever seizures
- Altered mental state.

Differentials

- Stroke
- Severe malaria
- Trauma
- Intoxication, particularly if focal signs are not prominent.

Investigations

- Full blood count
- Renal function tests
- Electrolytes
- Liver function tests
- Blood Culture
- Malaria parasite slide/RDT for malaria
- Lumber Puncture, if not contradicted
- Neuroimaging, if indicated
- EEG if suspicion of non-convulsive status epilepticus

Management

- Admit patient to High Dependence Unit (HDU)
- Stabilize the patient (airway, breathing, circulation, disability)
- Correct hypoglycaemia
- Control hyperthermia with anti-pyretic
- Manage seizures with appropriate anti-seizure medication
- Monitor vitals and Glasgow coma scale 4 hourly -look for signs of increased intracranial pressure
- Adequate hydration with isotonic fluids at least two third of requirements to guard against cerebral oedema and syndrome of inappropriate ADH secretion
- Institute empirical antibiotics (adequate coverage for encapsulated organisms like X-pen and chloramphenicol or third generation cephalosporins).

References

1) Ochocinski D, Dalal M, Black LV, et al. **Life-Threatening Infectious Complications in Sickle Cell Disease:** *A Concise Narrative Review. Frontiers in Pediatrics* 2020; 8: 38.

9. Major surgery in persons with SCA

Persons with SCA are more likely to undergo surgery than the general population. Surgery exposes patients to the factors that precipitate RBC sickling, Thus SCA patients undergoing surgery require meticulous clinical care to prevent peri-operative sickle cell disease-related complications. Even with meticulous care, approximately 25% to 30% of patients will have a post-operative complication.

Patients ought to receive simple transfusion to reduce sickled red cells and achieve haemoglobin of 10g/dL and rehydration intravenously at 1.25 x (the maintenance the night before surgery).

Risk factors for complications

- Dehydration
- Infection
- Acidosis
- Hypoxia
- Hypothermia

All these factors may precipitate vaso-occlusive crises and other complications, and therefore should be looked for and treated.

NOTE: sickle cell patients should not be transfused to Hb >10 g/dL or Hct > 30% as this results in increased risk for stroke and vaso- occlusion

Investigations:

- FBC and differential
- Reticulocyte count
- Chest X- ray
- Group and cross match
- Complete metabolic panel.

Management

Pre-operative

- Ensure HB of 9.5-10g/dl, pre-operative, in case of elective major cases.
- Platelet transfusions as appropriately indicated.
- Keep patient warm pre-operative.
- Hydrate the patient with intravenous fluids - warm where possible- during fasting periods.
- Monitor the patient's vital signs and pulse oximetry.
- Assess pain /document specific pain scale *(appendix)*
- Administer pain medication/antibiotics/blood products as needed
- Assess for and document adverse reactions to previous anaesthesia administration.

Intra-operative

- Apply measures to prevent hypothermia.
- Hydrate the patient with Intravenous fluids
- Monitor the patient's vital signs and pulse oximetry.
- Monitor any blood loss by weighing sponges and document blood loss, communicating to the surgeon and anaesthesia team
- Intra-operative laboratory assessment as needed

Post-operative

- Assess laboratory test values
- Correction of metabolic state,
- Correct anaemia as needed
- Prevent hypothermia by keeping the room warm.

- Hydrate the patient with IV fluids and encourage oral fluids intake as soon as possible
- Monitor the patient's vital signs and pulse oximetry
- Assess pain and administer pain medication if indicated.
- Physiotherapy and early ambulation as applicable.
- Provide patient and family member education
- Post-operative antibiotics

Reference

1) Lisa Fisher, **Perioperative Care of the Patient with Sickle Cell Disease,** *www.aorn.org/CE,*

10. Acute abdomen in SCA

Acute pain emanating from abdominal organs will present with the acute abdomen. The abdomen may be tender with guarding and rigidity and can be difficult to distinguish from the surgical acute abdomen. Such presentation may be deemed VOC with consequent delay in diagnosis and treatment of a condition requiring surgical treatment.

Clinical features

- Acute abdominal pain,
- Pyrexia,
- Abdominal tenderness/rigidity/guarding
- Reduced bowel sounds
- Constipation,
- Vomiting
- Worsening jaundice
- Haematuria/Proteinuria
- Severe anaemia
- Dysuria
- Rebound tenderness

Differential diagnosis to include:

- Urinary tract infection (UTI)
- Ovarian cyst
- Ectopic pregnancy
- Acute appendicitis
- Pancreatitis
- Cholelithiasis/cholecystitis
- Acute hepatic sequestration
- Acute hepatitis
- Splenic abscess
- Peritonitis secondary to bowel perforation e.g. typhoid
- Constipation secondary to opioid use

Investigations

Based on the differential diagnosis for the cause of the acute abdomen and may include the following:

- Laboratory investigations:
    - Urinalysis
    - FBC
    - Amylase
    - LFTs
    - Blood culture
- Radiological:
    - Ultrasound
    - X-Rays
    - CT/MRI when available

Management

The management will be based on the clinical, laboratory and radiological confirmation of the cause of the acute abdomens.

- In abdominal VOC, management should be conservative:
- Adequate hydration
- Pain management is required.
- Antibiotics in the case of UTI, appendicitis, cholecystitis, splenic abscess, peritonitis

- Surgical management if indicated
- Guidelines pre and perioperatively to be followed as above for MAJOR SURGERY

Reference

1) Jebbin N J, Adotey J M. **Acute abdominal conditions in people with sickle cell disease: A 10-year experience in Port Harcourt, Nigeria.** *Ann Afr Med* 2011; 10:165-70.

11. Avascular necrosis of femoral (ANFH) or humeral head

Avascular necrosis (AVN) is as a result of intravascular sickling of red blood cells in the micro - circulation of the bone. This causes intramedullary sludging, stasis, thrombosis, destruction of the vessel walls, oedema, and progressive ischaemia leading to necrosis of femoral/humeral head. These processes lead to symptoms of chronic pain of joints affected and later develop limb length discrepancies and restricted movement. AVN located only in the epiphysis

Clinical features

- Painful hip which manifests as groin pain, referred pain to knee or leg. The pain is initially felt on movement then later at rest and is recurrent or persistent (>8wks).
- Limitation of movement
- Abnormal gait (antalgic and/or shot limb gait)

Differential diagnosis:

- Osteomyelitis (Acute vs Chronic),
- Septic arthritis,

Investigations:

- FBC
- Blood Cultures
- Ultrasound
- X- ray. Radiological changes seen on X- rays. Pathologic changes in the femoral head, osteochondritis dissecans, coxa vara, spontaneous fracture,
- MRI

Management:

- Prevention and management of femoral head AVN must include medical treatment to reduce the occurrence of painful vaso-occlusive crises, which are known to trigger femoral head AVN.
- Identify risk factors and early evaluation of all cases of hip pain (especially >6-8wks).
- Preventative measure to include hydration and pain control to manage painful joint crises.
- Conservative treatment includes: Bed rest, traction, non-weight-bearing, bracing, and physiotherapy before femoral head AVN has appeared as noted on X- rays/MRI.
- Surgical treatment for advanced cases requires referral to an orthopaedic surgeon and may include femoral or pelvic osteotomies, core decompression, hip arthrodesis (joint fusion), and total hip arthroplasty
- Hydroxyurea and blood transfusion cannot reverse process but can prevent progression to contralateral joint.
- Pre-operative and post-operative transfusions for 3 months can maximise bone healing.

References

1) RM Musowoya, P Kaonga, A Bwanga et al. **Predictors of musculoskeletal manifestations in paediatric patients in presenting with sickle cell disease at a tertiary hospital in Lusaka, Zambia.** *Bone Joint Open* 2020; 1-6: 175-181

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3) Akakpo-Numado G. **Osteoarticular complications of sickle cell disease in children.** *Hard Tissue*. 2013;2(3). doi:10.13172/2050-2303-2-3-486

12. Osteomyelitis

Acute or chronic bone infection affecting the metaphysis of bone. The commonest site of Osteomyelitis is usually the lower limbs, especially the Tibia. Staphylococcus aureus is the commonest causative organism. However, Salmonella infection is also common in SCD. It is important not to miss the acute stage of osteomyelitis because this helps prevent serious long-term orthopaedic sequela caused by chronic osteomyelitis. Also note that it is very difficult to distinguish between acute osteomyelitis and bone infarctions caused by VOCs.

Osteomyelitis can be classified as acute, post-acute and chronic depending on the duration and presentation. Subacute osteomyelitis should be distinguished from post- acute as this is a type of osteomyelitis that is caused by less virulent organisms.

Clinical features

Acute Osteomyelitis:

- Fever or chills
- Irritability or lethargy in young children
- Pain in the area of the infection
- Swelling
- Warmth and redness over the area of the infection
- Loss of movement
- Sometimes no signs and symptoms or
- Have signs and symptoms that are difficult to distinguish from other problems such as VOC.

Post-acute osteomyelitis:

- Same as acute stage with increased bone pain
- Possible pyomyositis (abscess).

Chronic osteomyelitis:

- Pus discharge from sinus
- Pathological fractures presenting as acute pain
- Deformity or
- Inability to bear weight on the affected limb.

Sub-acute osteomyelitis:

- Uncommon infection with bone pain
- Radiographic changes without systemic symptoms
- It is usually caused by indolent bacteria
- Characterised by a Brodie's abscess on imaging.

Differential diagnosis

- VOC (Bone infarctions)
- septic arthritis
- Local skin infection/ Pyomyositis (abscess)
- Tumour

Investigations

- FBC,
- Blood cultures,
- CRP/ESR

- X- rays (Changes in osteomyelitis do not appear until about 10 days after the onset of symptoms which coincides with the post-acute stage)
- Ultrasound/MRI in acute episodes are difficult to assess
- Joint aspiration for culture of septic arthritis (never aspirate an affected joint without prior consultation with a consultant).

Management:

Acute osteomyelitis should be managed medically with antibiotics and no surgical intervention is required cloxacillin, if gram stain shows gram-negative bacilli - add a third-generation cephalosporin, ciprofloxacin can also be used especially when we suspect Salmonella species. Note that the total duration for antibiotic administration should be for at least 4 – 6 weeks which should include 1-2 weeks of intravenous administration.

- Serial infection markers should be done to monitor antibiotic response. Note that ESR is less reliable in neonates and sickle cell patients.
- Hydration
- Pain management
- Rest of limb
- Orthopaedics consultation: For post-acute and chronic osteomyelitis
- Bone drilling if acute (to relieve the exudate and hence pressure in the medullary cavity to prevent bone death; sequestrum formation) and post-acute osteomyelitis (to reduce the pressure from the accumulated pus within the medullary cavity of the bone).
- Splintage of affected limb with Plaster of Paris (POP) or traction for pathological fractures prior to referral
- Medical and surgical teams will work in liaison.

References

1) Akaro IL, Madewo G, Orwotho N, Nankund J, Byanyima R, Samoyo PTK. **The prevalence and factors associated with musculoskeletal disorders, in patients with sickle cell anaemia, at Mulago National Referral Hospital, Uganda.** *East and Central African Journal of Surgery*. 2016;21(1):96-112.

2) Nwadiaro HC, Ugwu BT, Legbo JN. **Chronic osteomyelitis in patients with sickle cell disease**. *East Afr Med J*. 2000;77(1):23-26.

3) Tekou H, Foly A, Akue B. **Current profile of hematogenous osteomyelitis in children at the Tokoin University Hospital Center in Lome, Togo.** Report of 145 cases]. *Med Trop (Mars)*. 2000;60(4):365-368.

4) Akakpo-Numado G. **Osteoarticular complications of sickle cell disease in children.** *Hard Tissue*. 2013;2(3). doi:10.13172/2050-2303-2-3-486

5) Doppelt E, de La Rocque F, Morriet Y, Reinert P. **Osteomyelitis in patient with sickle cell disease**. *Arch Fr Pediatr*. 1990;47(10):715-720.

6) Onwubalili JK. **Sickle cell disease and infection.** *J Infect*. 1983;7(1):2-20. doi:10.1016/s0163-4453(83)90863-0

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13. Septic arthritis

Sickle cell patients are susceptible to bone and joint infection due to

- Hyposplenia, asplenia
- Sluggish circulation
- Decreased opsonisation of bacteria

Clinical features

- Bone and joint pain
- Joint swelling with inflammation
- Fever

Investigations

- Elevated CRP and ESR
- Raised white blood cell (WBC) count with neutrophilia
- Aspirate joint in consultation with the consultant and under strict aseptic conditions and culture to identify organism (preferably refer to Orthopaedic surgeons for this)

Treatment

- Antibiotic regime as for acute osteomyelitis
- Arthrotomy of the joint by orthopaedic surgeons
- Hydration
- Preoperative oxygen prior to surgery to prevent sickle cell crisis

References

1) Akaro IL, Madewo G, Orwotho N, Nankund J, Byanyima R, Samoyo PTK. **The prevalence and factors associated with musculoskeletal disorders, in patients with sickle cell anaemia, at Mulago National Referral Hospital, Uganda.** *East and Central African Journal of Surgery*. 2016;21(1):96-112.

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14. Chronic skin ulcers

A common complication of skin necrosis secondary to VOC or decubitus ulcers in bed ridden individuals

Clinical features

- Erythema,
- Pain
- Dermal gangrene

Differential diagnosis

- Any skin infections

Investigations

- FBC,
- ESR,
- Pulse oximetry
- Pus swab for M/C/S

Management

- Conservative treatment aimed at keeping ulcer clean by regular daily dressings.
- Bed rest is essential
- Surgical debridement of thick slough at bedside with analgesia, sedation and local anaesthesia
- Local therapy for small-size ulcers: soaks, salves, gel boots, topical zinc, steroids, antibiotics creams
- Surgical procedures reserved for non-healing ulcers or large size > 8 cm. A high recurrence rate of 52%
- Split skin/ full-thickness grafts required. Pinch grafting has the advantage of being a minor procedure that can be performed under local anaesthesia (LA) and repeated, as necessary
- Hydroxyurea and recombinant human erythropoietin improve healing by promoting ulcer healing
- Counselling and patient education on wound care necessary

Reference

1) Caterina P. Minniti, James Eckman, Paola Sebastiani et al. **Leg Ulcers in Sickle Cell Disease.** *Am J Hematol*. 2010 October; 85(10): 831–833. doi:10.1002/ajh.21838
2) Kara-Marie H. Delaney, Karen C. Axelrod, Ashley Buscetta et al. **LEG ULCERS IN SICKLE CELL DISEASE: CURRENT PATTERNS AND PRACTICES.** *Haemoglobin.* 2013; 37(4)

15. Cholecystitis and cholelithiasis

Cholecystitis is a common complication in SCA. This is primarily due to cholelithiasis which is very prevalence in SCA due to chronic haemolysis (30% all patients) that results in a high bilirubin turnover. In SCA patients, stones are usually asymptomatic but can precipitate painful abdominal crises.

Clinical features

- Right upper quadrant abdominal pain
- Pyrexia
- Jaundice

Differential diagnosis:

- Hepatic sequestration (cholestasis)
- Hepatitis
- Girdle syndrome
- Acute chest syndrome
- Acute pancreatitis
- Peptic ulcer disease

Investigations:

- FBC
- Blood culture
- LFTs, AST, ALT, LDH, GGT and ALP
- Abdominal Ultrasound,
- Abdominal X- ray,
- CT abdomen when available

Management:

- Initially management in the acute phase is conservative with antibiotics (Metronidazole/Cefotaxime),
- Pain management
- Hydration
- Bowel rest NPO
- Asymptomatic patients with cholelithiasis may not need immediate treatment and need follow-up.
- Once the acute phase is passed the treatment is surgical: Cholecystectomy

Reference

1) Rushikesh Shah, Cesar Taborda, Saurabh Chawla. Acute and chronic hepatobiliary manifestations of sickle cell disease: A review. World J Gastrointest Pathophysiol 2017 August 15; 8(3): 108-116

CHAPTER 7: SICKLE CELL DISEASE IN PREGNANCY

With improved care many female SCD patients have grown to reproductive age posing a challenge of managing sickle cell patients in pregnancy. SCD is associated with both maternal and foetal complications and is associated with an increased incidence of perinatal mortality, premature labour, foetal growth restriction and acute painful crises during pregnancy. Some studies also describe an increase in spontaneous miscarriage, antenatal hospitalisation, maternal mortality, delivery by caesarean section, infection, thromboembolic events and antepartum haemorrhage. An increased risk of pre-eclampsia and pregnancy-induced hypertension has been described in some studies. In HbSC there are fewer reported adverse outcomes, but there is evidence of an increased incidence of painful crises during pregnancy, foetal growth restriction, antepartum hospital admission and postpartum infection.

Diagnosis:
Diagnosis of SCD is usually made in childhood. If not already diagnosed in childhood, the initial screening test available is a sickling/solubility or sickle-scan test. The final diagnosis is by use of haemoglobin electrophoresis, isoelectric focusing (IEF) or High-Performance liquid chromatography (HPLC).

Note: Routine screening for SCD should be done prenatally or during antenatal for those that do not know their sickle cell disease status

Management:

1. **Prenatal**

Patients should be counselled on the risks of sickle cell disease in pregnancy. Premarital genetic counselling and screening of the couple is important in high SCD prevalence settings or husband or partner screening should be conducted if one partner is recently diagnosed. A multi- disciplinary team comprising physicians and haematologist should be involved in the management of the patients, so that the patient is in good state of health before pregnancy is attempted. Other measure to put in place are:

- Folic acid (5 mg) should be given once daily both pre-conceptually and throughout pregnancy
- Need to check that all the medications the patient is on are not teratogenic.
- Hydroxycarbamide (hydroxyurea) should be stopped at least 3 months before conception.
- Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) should be stopped before conception.
- Hepatitis B vaccination is recommended, and the woman's immune status should be determined pre-conceptually.
- Women with SCD should be advised to receive the influenza and 'swine flu' vaccine annually
- Contraception should be advised in case the woman is not ready for pregnancy.

2. **Antenatal**

Patients are advised to start antenatal care as soon as the diagnosis of pregnancy is made. The women should be offered a viability scan at 7–9 weeks of gestation, the routine first-trimester scan (11–14 weeks of gestation) and a detailed anomaly scan at 20 weeks of gestation. In addition, serial foetal biometry scans (growth scans) every 4 weeks from 24 weeks of gestation should be done.
The following also need to be done:

- Avoid precipitants of painful crisis such as a cold environment, excessive exercise, dehydration
- Mild pain may be managed with rest, oral fluids and paracetamol or weak opioids. Non-steroidal anti-inflammatory drugs (NSAIDs) should be used only between 12 and 28 weeks
- Influenza vaccine should be recommended if it has not been administered in the previous year.
- Baseline full blood count (FBC), Urea and electrolytes (U&Es)
- Urinalysis should be performed at every visit and urine culture monthly to screen for urinary tract infections.
- Folic acid and anti-malarial medication

- Ferrous sulphate should not be given prophylactically (only in proven cases of Fe deficiency)
- Antibiotic prophylaxis with Penicillin or the equivalent should be prescribed for encapsulated bacteria in those who are not vaccinated.
- Low dose aspirin 75mg should be given from 12 weeks in order to reduce the risk of pre-eclampsia and thromboembolism.
- Should receive low molecular weight heparin (LMWH) in case of antenatal admissions.
- Should be advised to take fluids, about 2 *litres* every day
- Women should also have monthly scans to monitor foetal growth.
- Offer anaesthetic assessment in the third trimester of pregnancy.
- Women with SCD who become unwell should have sickle cell crisis excluded as a matter of urgency.
- Pregnant women presenting with acute painful crisis should be rapidly assessed by the multidisciplinary team and appropriate analgesia should be administered. Pethidine should not be used because of the associated risk of seizures.
- Women admitted with sickle cell crisis should be looked after by the multidisciplinary team, involving obstetricians, midwives, haematologists and anaesthetists.
- The requirement for fluids and oxygen should be assessed, so that they are administered if required.
- Thromboprophylaxis should be given to women admitted to hospital with acute painful crisis.

3. Labour and delivery

Pregnant women with SCD who have a normally growing foetus should be offered elective birth through induction of labour, or by elective caesarean section if indicated, after 38+0 weeks of gestation. SCD should not in itself be considered a contraindication to attempting vaginal delivery or vaginal birth after caesarean section. The relevant multidisciplinary team (senior midwife in charge, senior obstetrician, anaesthetist and haematologist) should be informed as soon as labour is confirmed. Blood should be cross matched for delivery if there are atypical antibodies present (since this may delay the availability of blood), otherwise a 'group and save' will suffice.

- In women who have hip replacements (because of avascular necrosis) it is important to discuss suitable positions for delivery.
- To be nursed in a high dependency ward
- Adequate analgesia should be given e.g. morphine (Avoid pethidine as it increases the risk of seizures (fitting) in SCD)
- Should be well hydrated
- Keep the patient warm
- May need transfusion if Haemoglobin is less than 7g/dl
- Active management of third stage
- Antibiotic prophylaxis after delivery.
- Continuous intrapartum electronic foetal heart rate monitoring is recommended owing to the increased risk of foetal distress which may necessitate operative delivery.
- Caesarean for obstetric indications
- Regional analgesia is recommended for caesarean section.

4. Postnatal

Women that missed screening for SCD or do not know their status after delivery should be screened in the postnatal period. Those whose babies are at high risk of SCD (i.e. the partner is a carrier or affected), should be offered early (new-born) screening for SCD.

Maintain maternal oxygen saturation above 94% and adequate hydration based on fluid balance until discharge. Low-molecular-weight heparin should be administered while in hospital and 7 days post-discharge following vaginal delivery or for a period of 6 weeks following caesarean section. The same level of care and vigilance should be maintained as has been described for antenatal care, since acute crisis and other complications of SCD remain a risk in the puerperium. Keep in the hospital for 24 to 48 hrs after delivery following a spontaneous

vaginal delivery. Should be counselled for family planning preferably progesterone only pill or Mirena. Oestrogen-containing contraceptives should be used as second-line agents.

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CHAPTER 8: BLOOD TRANSFUSION IN SICKLE CELL ANAEMIA

Blood transfusion is the administration of blood or blood derivatives via the intravenous route. Blood transfusion has become a major treatment option in SCA with increase in indications for its use and increasing evidence of its benefits. Transfusion effectively reduces the percentage of circulating sickled erythrocytes with abnormal haemoglobin. It may, therefore, be used in acute circumstances of severe anaemia, and in chronic states to prevent occurrence of complications. Blood transfusion is indicated when the haematocrit is below 15 or to maintain an Hb of 10g/dl when surgery is indicated.

Indications for Blood Transfusion

The following are some of the conditions where blood transfusion in SCA is indicated:

- Acute Chest Syndrome (exchange transfusion) [NEJM 2000; 342:1855–1865]
- Recurrent stroke (exchange transfusion) [NEJM 1998; 339:5–11]
- Surgery (simple transfusion) [NEJM 1995; 333:206–213]
- Splenic (and hepatic) sequestration (simple transfusion)
- Aplastic episode (simple transfusion)
- Sepsis (simple transfusion)
- Multiorgan failure (exchange transfusion)
- Recurrent VOC- definition of recurrent VOC refer chapter 5
- VOC not responding to conventional pain therapy
- Acute anaemia
- Surgery

Complications of blood transfusion

Unfortunately, the administration of blood and blood products presents with risks for patients, some of which can be life threatening. Some of the risk are.

- Infection. All blood in Zambia is tested for infections including HIV, Hepatitis and syphilis.
- Alloimmunization/delayed haemolytic transfusion reactions/hyperhaemolysis. To reduce alloimmunization the doctor could request units with minor antigens
- Acute transfusion reactions
- Iron overload

Some of these complications occur with chronic transfusion or excessive transfusion in an emergency situation. Either way, it must be kept in mind that blood transfusion is not altogether free of problems and the physician should weigh the risk benefits ratio when deciding to transfuse. It is, therefore, prudent to minimize the deleterious effects of blood transfusion by following guidelines laid down by the blood bank in the selection of blood products and the infusion of blood to patients with SCA. Generally, the indications for transfusion should help guide the decision-making process, though collaboration with the blood bank would be of great help. For instance, it is important to have and document important baseline results if you can, however the challenge is that most facilities lack capacity for timely results for decision making.

However, if able to, before transfusion is given the following should be documented

- FBC
- Ferritin Levels
- Reticulocyte count
- X-Match

To determine how much blood is to be transfused the formulae below may be use:

For a simple blood transfusion:

Blood transfused (BT)= (Desired $_{Hb}$ - Actual$_{Hb}$) x Total Body Weight x K

K=4 for Packed cells
K=6 for whole blood

And for Exchange Transfusion:

Volume of blood (ml) x 100 = (Desired$_{Hb}$ - Actual$_{Hb}$) – (Total Body Weight) x 3

If weight above 50 kg

Blood transfused = Desired$_{Hb}$ - Actual$_{Hb}$

NOTE: Desired – actual = Deficit

Hyper-transfusion therapy

Hyper-transfusion therapy in SCD is a chronic blood transfusion regimen aimed at reducing the sickle cell haemoglobin (HbS) levels in the peripheral blood over a long period of time. It can be done as frequent top-up transfusions (Appendix 2) or as exchange transfusions.

Indications for hyper-transfusion therapy in SCD

- Prevention of stroke (Transcranial doppler ultrasound with cerebral blood flow>2m/s which is highly predictable of stroke)
- Prevention of repeat stroke
- Recurrent vaso-occlusive crises in the bones requiring 3 or more hospital admission/year and are not responsive to hydroxyurea therapy
- Recurrent acute chest syndrome unresponsive to hydroxyurea therapy
- Pregnant SCD patients with previous bad obstetric history
- Delayed growth and development in children with SCD

References

1) Ademola S Adewoyin and Jude C Obieche. **Hyper transfusion Therapy in Sickle Cell Disease in Nigeria**; *Advances in Haematology* Volume 2014, Article ID 923593, 8 pages http://dx.doi.org/10.1155/2014/923593

CHAPTER 9: ADOLESCENTS, SEXUALITY AND PRE-MARITAL COUNSELLING

The Paediatrician's role of looking after children from the womb to the tomb also encompasses the need **to promote and advocate for safe childhood in an unsafe world.** During adolescence, individuals often experience significant internal turmoil secondary to physiologic changes in body habitus, as well as changes in the way they and society perceive each other. The adolescent strives to achieve the independence of adulthood while clinging to the security of childhood. Among the issues that adolescents must confront are those related to personal and sexual identity, their sense of self-worth, and their role in society. Therefore, it is important that children and adolescents are well equipped with information on key issues that affect them. As SCD affects many aspect of a person's life, it is imperative that all children and adolescents, particularly those living with the condition, are imparted with knowledge about the condition, to enable those who may know someone with the condition, deal with them with appropriate patience and understanding, and for those with the disease to face the world with more confidence and self-esteem.

Adolescents with SCD must face each of these challenges, as well as the difficulties related to their chronic illness. In addition to becoming an adult, adolescents with SCD also must accept primary responsibility for the management of SCD. Physicians caring for adolescents must be sensitive to all the problems these patients are experiencing, and they must be willing to help guide them during this difficult transition period.

Issues needing special attention

1) Delayed puberty - it is imperative to let them know that puberty will be delayed and for girls their menstrual cycle may delay for some months, even years. Assurance must be given that this is normal for the condition, and issues of insecurity that may come with this must be dealt with as much as possible.
2) Physical limitations due to SCD – During a period when older children and adolescents would want to "fit in" and go out with their peers, getting regularly sick and in need of medical attention can lead to depression. This could lead to self-neglect, difficulties with adhering to prescribed medication and other issues, which could make the situation worse. It is important that signs of depression are identified early, and appropriate care is sought. It is also important to note that depression is generally common among 'healthy' adolescents and this should also be emphasized so that the older child or adolescent understand.
3) Pregnancy – As much as possible, adolescents should be regularly counselled about the need to prevent unwanted pregnancies. It is also important to remind them about the possibility of having a child with the condition and therefore be counselled about the need to know the sickle cell status of their potential sexual partners. Key, however, are issues of delaying sexual debut, safe sex as well as contraception use. These also apply to other adolescents as well.
4) Priapism (painful, long-lasting erections) - Boys should be counselled on this condition and the need to inform their trusted care givers and go to seek medical attention immediately.
5) Transition of care: Mechanisms for transferring care from the paediatrician to adult care – every health facility should put in place mechanisms of ensuring this process is handled well in order to ensure continued care for adolescents as they transition to adult care. The University Teaching Hospitals-Children's Hospital has introduced a transition protocol for all paediatric patients with chronic disease and currently putting the protocol into practice (Appendix 6)

CHAPTER 10: SICKLE CELL DISEASE AND THE COMMUNITY

SCD is a public health problem in Zambia and as such requires a comprehensive approach that not only involves management in health facilities, but strategies for prevention, management, and surveillance at community level as well. As with all chronic disorders, improved care creates a cumulative demand for more services. Surveillance and education must be delivered at the community level through the primary health-care system, so as to increase public awareness of the problem and lengthen the survival of affected individuals. This therefore calls for capacity building of the primary health care facilities and Community Health Care Workers, in order for them to give appropriate counselling to members of the general public. Community Health Workers (CHWs) are an important link between the household and the health facility. Studies have shown that a community-based health workforce contributes to improved management of health conditions and with the right training are an important resource for the management of SCD at community level. Zambia is currently scaling up the number of trained CHWs in the country, with an aim of saturating health facility catchment areas with a ratio of one CHW per 500 people. Ideally trained CHWs should play a role in strengthening prevention and management of SCD at the community level.

It is also important that families are encouraged to form support groups that have been known to play a big role in further awareness raising, as well as a source of support and information to the patients and their families.

Prevention

Sickle-cell anaemia can be prevented. Prevention with absolute certainty entails not having children. It also entails setting up genetic counselling services (see Chapter 12) and early screening interventions Knowledge of the SCD status, leads to identification of people who carry the sickle cell gene, and are at risk of having affected children. Information of the carrier or disease state can be used to counsel couples preparing to marry and to have children. Those with the disease or carrier trait that decide to have children can be offered necessary counselling to have their children tested as early as possible and to be linked to lifesaving follow up interventions. Counselling should also involve early identification of signs and symptoms, and the necessary home management of sickle cell patients.

An effective SCD screening programme should be implemented in conformity with the three core principles of medical genetics:

1) *The autonomy of the individual or the couple.*
2) *Their right to adequate and complete information, and*
3) *The highest standards of confidentiality.*

Management

Health education focusing on the management of SCD at community level must be delivered through the primary health-care system and community health workers. Health education has been demonstrated to be effective in reducing SCD mortality in young children, preventing complications, and maintaining health through the life cycle. This includes increasing knowledge to prevent dehydration, avoiding severe cold/heat, preventing infections, maintaining appropriate nutrition, recognizing symptoms, and seeking treatment early for symptoms which require medical attention. As such, capacity building of CHWs and other community level structures and volunteers is needed. CHWs and others can provide appropriate information to members of the general public. In addition, it is imperative that Information, Education and Communication (IEC) materials containing correct information about the management of SCD are disseminated. Mass media and other appropriate channels can also be used to complement community level activities.

Health education is also instrumental for addressing common myths and misconceptions associated with SCD and decreasing stigma. Health education and counselling should aim at providing facts, dispelling myths and misconceptions, as illustrated below:

Facts about SCD

1. **SCD is a life-long illness.**

   TRUE: The presence of SCD is known at birth. It is a life-long illness that can be managed. The disease affects people differently and the severity differs from person to person. Early diagnosis, regular medical care by a qualified doctor and awareness of pain triggers all contribute to improved quality of life for patients with the disease.

2. **SCD can cause severe pain crises in patients.**

   TRUE: Common activities and normal circumstances can bring on sudden, severe pain crises in people with SCD. Any activity that decreases the amount of oxygen in a person's body can abruptly change RBCs from round-shape to sickle-shape, thereby increasing likelihood the sickle cells getting stuck in tiny blood vessels and clogging the blood flow.

   The intensity of the pain varies from person to person and can last for a few hours, up to a few weeks. Some people may only have a few pain episodes in their lifetime, while others will have a dozen or more crises a year. (Mayo Clinic, 2017)

   Typical circumstances that might bring on a severe pain crisis in a person with SCD are fever, vomiting or diarrhoea causing dehydration, fatigue, stress, extremely cold weather, profuse sweating in hot weather, and pregnancy. Common activities that have also been known to cause a pain crisis are swimming underwater, flying at a high altitude, squatting down, heavy or excessive exercise, and prolonged labour during childbirth.

3. **Sickle cell patients have delayed puberty**

   True: Sickle cell patients have delayed puberty because of slow growth rate experienced by most sickle cell patients. While people without sickle cell begin their mensuration at 13/15 years, most sickle cell patients will often start their periods at 18/19 years.

Myths and Misconceptions on SCD

1) **Only black people suffer from SCD.**

   FALSE: SCD does not discriminate based on ethnicity or skin colour. It occurs more often among people from regions of the world where malaria is common. Millions of people from around the world are affected by this disease, especially those whose ancestors descended from sub-Saharan Africa, Saudi Arabia, India, the Mediterranean (Greece, Sicily and Turkey), and Latin countries in South and Central American. (Centres for Disease Control and Prevention, 2016).

2) **SCD is a contagious blood-borne disease like HIV and Hepatitis B.**

   FALSE: SCD is genetic condition present at birth. It is inherited when an offspring receives the sickle cell trait from **both** biological parents. Therefore, a child can **only** have SSCD when both of his/her parents have the abnormal haemoglobin gene. A person cannot become "infected" by the blood of someone who has SCD, or who carries the sickle cell trait. SCD is not contagious.

3) **All RBCs have the same properties.**

   FALSE: Sickle haemoglobin is not like normal haemoglobin. Most RBCs are round in shape (like a disc) so they can flex through blood vessels of all sizes to deliver oxygen. However, in sickle haemoglobin, the RBCs become hard and sticky and look like a C-shaped farm tool called a "sickle." The sickle cells have difficulty transporting oxygen due to their sickle shape; they often get stuck and clog the blood flow in tiny vessels. This can cause pain and other serious problems.

4) **People with the SCD are immune to malaria.**

FALSE: While scientists believe that SCD is an evolutionary response to malaria, people with SCD do not have the benefit of this evolutionary mutation. Many doctors have been known to tell patients with SCD that they are immune to malaria and do not require anti-malarial protection. This is not true and puts patients at a greater risk. However, there is some evidence to suggest that people who carry the sickle cell trait, but did not inherit the gene from both parents, are less likely to have severe forms of malaria and may have higher childhood survival rates.

5) **Sickle cell skips a generation.**

FALSE: Sickle cell is an autosomal recessive disorder. This means that both parents must carry the sickle allele (gene) to have a child with sickle cell disease. To carry the gene, the parents could themselves have sickle cell disease, or be carriers (have sickle cell trait, but not sickle cell disease). For more information, see the “About Sickle Cell” page, and watch the video “How is sickle cell disease inherited?”

6) **Sickle cell patients do not grow to adulthood.**

FALSE: In the past, sickle cell patients often died from organ failure, infection and other complications at an early age. Today, people with sickle cell disease can live into their 50s and beyond, thanks to modern medicine. The most recent in-depth study on mortality and causes of early death in sickle cell disease was published in 1994. This study determined average life expectancy to be 42 years for males and 48 years for females in the United States (Platt et al., 1994). In the UK, the current estimate is between 53 and 60 years of age. That is not to say that people with sickle cell disease cannot live past 60. Indeed, people with sickle cell disease can live into their 80s. See the “Healthy Living” page for tips on how to live a long, healthy and happy life with SCD.

7) **Sickle cell patients are mentally challenged.**

FALSE: Most people with sickle cell disease fall within the normal intelligence range. In a study of 60 SCD patients and 60 matched controls (people without SCD), the average IQ of SCD patients was 5.6 points lower than the controls. The average height of SCD patients was also lower than that of the controls, and height was shown to be correlated with IQ. The authors speculated that early factors, like nutrition, could have contributed to both slower growth and mental development in sickle cell patients (Knight et al., 1995). A meta-analysis of sickle cell studies showed that there were small but reliable differences in IQ between SCD patients and healthy controls. The authors of this study suggested that the differences could be due to effects of SCD directly on brain function or due to the effects of having a chronic illness on the brain more generally (Schatz et al., 2002).

8) **There is no cure for sickle cell disease.**

FALSE: Bone marrow transplantations have been successful, in some cases, in curing sickle cell disease. The bone marrow donor is usually a sibling with the same bone marrow type as the patient. Unfortunately, only 1 in 10 sickle cell patients is able to find a matching donor. Fortunately, there are other treatments that have been successful in managing SCD

9) **SCD is the same in every patient**

FALSE: The severity of sickle cell patients differs from patient to patient. This is because of the different levels of abnormality in the haemoglobin cells. While some patients can have crisis pain on a frequent basis, some patients can go years without crisis pain. In addition, some patients can have sickle cell distinct features while others do not have any features, so much that one cannot even tell they have SCD. The same applies to SCD complications, some patients can have strokes some do not. Medical personnel must equally learn to treat SCD as individuals, case by case and not as a uniform treatment requirement.

10) People living with SCD cannot have children

FALSE: This is not true, there is no connection between SCD and the reproductive system of a SCD patient. However, a person living with sickle cell is at high risk of complications during pregnancy because of low haemoglobin levels. They are more prone to suffer anaemia, hence posing a risk to the mother and the child. With strict Doctor appointments and medical follow ups as well as medication, a person living with sickle cell can a have a normal pregnancy and delivery.

11) Sickle cell patients are lazy

FALSE: Many sickle cell patients have recurrent bouts of pain, pain episodes include sickle cell crisis, migraines, hip pain caused by AVN, and joint pain. Other complications like anaemia cause sickle cell patients to experience tiredness, breathlessness, from time to time. As a result, it slows down their ability to do day-to-day activities. This does not mean they are lazy. Their bodies have not been built to handle stressful situations and physically demanding jobs. However, on their good days they are able to carry out their normal routine duties. Sedentary work is most ideal for sickle cell patients and healthcare workers are encouraged to advise their patients to consider jobs which are ideal for their lifestyle.

Role of Community-Based Organisations focused on SCD

Community-based organizations (CBOs), are important health system stakeholders as they have the ability to provide valued programs and services to the members of their community. There are benefits to having CBOs focused on SCD in Zambia. CBOs can help individuals manage their chronic diseases and meet their often-overlooked social needs. CBOs can help improve patient outcomes through health education thus preventing unnecessary hospital admissions. CBOs which have been created to support the needs of those living with SCD and their families already exist in Zambia. These groups have great potential to double the efforts of MOH.

CBOs use diverse terminology to describe their organisations e.g. Societies, Foundations, Associations, not-for-profit but are essentially the same. CBOs will be encouraged to work closely with the Provincial Health Office (PHO). Once the PHO identifies the various CBOs operating within their jurisdiction, they must ensure that CBOs are working in a complementary and non-duplicative fashion. Ideally, CBOs should be encouraged to develop a joint, harmonised work plan. By doing so they will be able to leverage resources and maximise geographic reach. PHOs can also play a role in linking the various CBOs to private sector partners and larger well established international and local non-governmental organisations, who can provide technical and material assistance to these CBOs. The national HMIS shows that SCD is present in all 10 provinces in Zambia therefore it would be ideal to encourage the formation of CBOs in all ten provinces. At the national level, CBOs can be engaged in health system decision-making through mechanisms like Technical Working Groups to enhance engagement with MOH in an orderly fashion

Advocacy

Some of the CBOs will also conduct advocacy activities to influence decisions within political, economic, and social institutions. Advocacy includes activities and publications to influence public policy, laws, and budgets by using facts, the media, and engagement of government officials and the public to facilitate civic engagement and social action. Advocacy can include many activities that the organization undertakes including media campaigns, public speaking and commissioning. An illustration of the key advocacy topics and activities are listed below:

1) *Raise reporting rates in public health facilities: Approximately 56.9% of public health facilities are currently **not** reporting into the national health management information system (HMIS), CBOs will advocate for an increase in this reporting rate.*
2) *Positively influence the perceptions of SCD patients: Quite often SCD patients face negative perceptions from health care workers when they ask for opiates to treat pain. CBOs will focus on advocacy activities to reduce the negative perception that people living with sickle cell are drug addicts*
3) *Include a more comprehensive module on sickle cell anaemia (including aspects of reproductive health in sickle cell) in all pre-service training for medical personnel*

4) *Advocate for an increase in the number of SCD clinics in the country, at least one in all teaching hospitals and tertiary (central, general) hospitals.*
5) *Engage Social Welfare Department under Ministry of Community Development to orient social workers on the social aspects of sickle cell. Social workers can educate care givers on positive lifestyle to promote improved care of people living with sickle cell.*
6) *Develop policies/guidelines to promote a smooth transitioning from paediatrics to adult care in hospitals.*
7) *Through MOH, engage Ministry of Education to develop policies/guidelines to increase awareness of sickle cell in schools, to promote a safe and supportive environment for learners who have SCD.*
8) *Engage institutions to fund and/or conduct research on SCD.*
9) *Advocate for the inclusion of hydroxyurea, folic acid (5mg), and any other SCD specific medication on the essential drugs list and secure funding to procure them and make them available in all public health facilities*
10) *Engage palliative care division to develop appropriate pain management guidelines for people living with SCD*
11) *Engage ZNBTS to increase availability of blood in all hospitals and to consider introducing exchange transfusions*
12) *MOH to consider avenues to leverage/piggyback on well-funded programs like malaria*
13) *MOH to develop annual costed work plans and include these budgets in the "yellow book"*
14) *Engage parliamentarians to support resource mobilisation activities*
15) *Strengthen the transitioning from paediatrics to adult care by providing same medical service, treatment and environment for sickle cell patients who are being moved from childcare to adult care*
16) *Counselling centres for sickle cell patients to provide counsel against the stigma, as well the transitioning of patients from child to adult. In addition, counselling programs for mothers who struggle with the reality of having a child with sickle cell.*

Community-based organisations involved with sickle cell disease

Foundation for People Living with Sickle Cell Anaemia

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Zambian Childhood Cancer Foundation (ZACCAF) / Haemophilia Foundation of Zambia HFZ

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Enriching Lives Through Hope

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CHAPTER 11: ESSENTIAL DRUGS FOR SICKLE CELL ANAEMIA

HYDROXYUREA

Mechanism of action: Hydroxyurea is an antineoplastic that may cause inhibition of DNA synthesis by acting as a ribonucleotide reductase inhibitor. It increases foetal haemoglobin, reduces neutrophils, alters adhesion of RBCs to endothelium, increasing water content of RBCs and increases deformability of sickled cells.

Benefits in paediatric patients with SCD include reduced rate of sickle-cell crises and reduced mortality. Benefits also include splenic preservation and long-term prevention of organ damage.

Use of hydroxyurea with erythropoietin enhances the production of foetal haemoglobin

Indications:

All patients with SCA (Hb SS) can benefit from hydroxyurea. Hydroxyurea has been shown to significantly decrease the number of vaso-occlusive episodes and episodes of acute chest syndrome, while also reducing the number of transfusions and hospitalizations. Newer studies suggest it may also provide some protection against overt stroke as well as other end organ damage. Recent studies have suggested that it lowers overall mortality as well. In infants (≥ 9 months of age), children, and adolescents with SCA, offer treatment with hydroxyurea regardless of clinical severity to reduce SCA-related complications.

If not readily available can be limited to patients with severe complications:

- ≥ 2 hospitalizations for Vaso-Occlusive Crises (VOC) episodes in a 12-month calendar period
- ≥ 1 acute chest crises requiring transfusion
- Significant # of days missed from school/work due to VOC pain managed at home regardless of # of hospital admissions
- Abnormal Trans Cranial Doppler (TCD) in patient refusing transfusion therapy
- Chronic hypoxemia
- Low haemoglobin < 7g/dL
- High conditional TCD velocities
- Presence of silent infarcts on screening
- Neurocognitive decline
- Poor growth and development
- Priapism
- Overt stroke*
- Pulmonary hypertension*
- Renal nephropathy*

* *Newer studies suggest it may also provide some protection against overt stroke as well as other end organ damage.*

Prior to initiating hydroxyurea please ensure the following are completed:

- Baseline investigations
- Patient education and ensure there is an ongoing discussion
- Develop a treatment plan

Prior to starting hydroxyurea ensure that the following is reviewed:

- Details of VOC episodes – number and severity
- Evidence of organ damage – TCD velocities, proteinuria, hypoxemia, academic performance
- Does the patient have sleep apnoea?

- Psychosocial issues which might impact compliance with treatment regimen such as transportation, and finances for drug coverage
- Document growth and development
- Thorough physical examination
- Document discussion, history and physical including height and weight, oxygen saturation, and laboratory reports

Patient and family involvement

- Discuss clinical effects
- Review of VOC episodes with family
- Discuss side effects
- Hematologic toxicity and beneficial effects
- Keep patient/family engaged in management. This improves compliance and instils confidence in taking the drug
- Celebrate beneficial effects and be open when toxicities occur.
- Show graphs of response e.g. MCV, HB F%.

Exclusions: acute liver disease, history of severe hydroxyurea toxicity or hypersensitivity, pregnancy or sexually active and unwillingness to use contraception.

Baseline investigations: FBC with Differential count, Hb electrophoresis with quantitative Hb F%), Chemistry profile, Liver function tests (AST, ALT), renal function tests (BUN, creatinine)

Consult with paediatrician for appropriate work- up before initiating a patient on hydroxyurea.

Dosing:

- The starting dose of hydroxyurea is typically 20-25 mg/kg daily by mouth.
- The dose is increased as tolerated to reach a target absolute neutrophil count (ANC) of between 2.0-3.0 x 10^9/L (obtained during “well” or steady state visits).
- The increase in hydroxyurea is usually done in increments of 3-5 mg/kg/day, adjusting the dose every 4- 6 weeks as tolerated.
- The usual effective dose in paediatrics is 26-28 mg/kg/day but can range from 20-30 mg/kg/day.
- A complete blood count (CBC) is monitored every 4-6 weeks during the period of dose escalation (usually the first 3 months), then every 3-6 months when on a stable dose.
- Increase dose until ANC 2,000- 3,000 achieved or 35 mg/kg/day dose achieved or evidence of haematological toxicity.
- Liquid formulation can be prepared by compounding pharmacy using published guideline.

Threshold for dose reductions

- Neutrophil ANC <2.0 x 10^9/L
- Retic count <80 x 10^{12}/L
- Platelets <80 x 10/L
- Haemoglobin <70 g/L

If haematologic toxicity occurs

Discontinue Hydroxyurea until counts recover (usually 5-7 days)

Restart at same dose. If threshold is again reached, reduce to previous dose and that is maximum therapeutic dose

Adverse effects

- CNS: Dizziness, disorientation, hallucination, drowsiness, seizures, headache, fever, chills, malaise.
- Dermatologic: maculopapular rash, facial erythema, thinning of the skin, pruritus, hyperpigmentation, vasculitis ulceration, gangrene, hair loss, nails changes.
- Endocrine and Metabolic: Hyperuricemia
- GIT: Nausea, vomiting, diarrhoea, constipation, anorexia, stomatitis, pancreatitis.
- Genitourinary: Dysuria, UTI
- Hematologic: Myelosuppression (leukopenia, neutropenia, thrombocytopenia), megaloblastic anaemia, bleeding.
- Hepatic: Hepatic enzymes elevated, hepatotoxicity.[18,19] Symptoms recur when the patients are re-challenged with hydroxyurea.
- Neuromuscular & skeletal: Peripheral neuropathy
- Renal: Renal tubular impairment, BUN elevated, serum creatinine elevated.
- Respiratory: Pulmonary fibrosis(rare), dyspnoea, pulmonary infiltrates
- Miscellaneous: Secondary leukaemia, skin cancer, parvovirus B-19 infection

Breast feeding

Hydroxyurea is distributed in breast milk and therefore women are advised not to breast feed while taking hydroxyurea

Interactions

- Antipsychotics: avoid concomitant use of cytotoxic with clozapine (increased risk of agranulocytosis)
- Antivirals: increased risk of toxicity when hydroxyurea given with didanosine and stavudine-avoid concomitant use
- Avoid concomitant use with natalizumab, live vaccines-increased levels(toxicity)
- Decreased levels of inactivated vaccines.
- Food interactions: in SCD patients' supplemental folic acid is recommended.
- HU may mask folic acid deficiency

Storage

Hydroxyurea is hygroscopic and decomposes in the presence of moisture. Therefore, it should be stored in airtight containers in a cool dry place. Protect from light.
Keep out of the reach of children
Compounded hydroxyurea syrup must be stored in a cool place and used within 14 days.

Other Essential Drugs For SCA

DRUG	DOSAGE	FREQ	COMMENT
Penicillin	2- 12mths: 62.5 mg PO 3yrs: 125mg PO >3yrs: 250mg PO	BD	Substitute with erythromycin if penicillin hypersensitivity present. Discontinuing penicillin prophylaxis can be considered for patients age 5 years and older who meet BOTH criteria: • Patients without prior history of documented pneumococcal infection • Patients who have received 1 dose of PPS (pneumococcal 23) and appropriate PCV 13 doses.
Folic acid	5mg PO	OD	Prophylaxis in chronic haemolytic states
Anti- malarial drugs			
Deltaprim	5yrs: 28.125mg PO 5- 10yrs: 56.25mg PO >10yrs: 112.5mg PO	Once weekly	Contains Pyrimethamine at 12.5mg and Dapsone at 100mg
Anti- malarial prophylaxis alternatives			
Proguanil	>12 wks., Wt < 6kg: 25 mg PO >12 wks, Wt 6-10kg: 50 mg PO 1-4 yrs., Wt 10-16kg: 75mg PO 4-8 yrs., Wt 16-25kg: 100mg PO 8-13 yrs., Wt 25-45kg: 150mg PO > 13 years, Wt >45kg: 200g PO	OD	Can be used alone for prophylaxis but is not suitable for treatment alone.
Malarone	Wt 5-8kg: 43.75mg PO Wt 8-10kg: 65.63mg PO Wt 10-20kg: 262.5mg PO Wt > 40kg standard adult tablet (350mg) PO	OD	
Other anti- malaria drug options			
Dihydroartentemisinin- piperaquine (DHAP) and, Mefloquine			

CHAPTER 12: VACCINATION OF SICKLE CELL ANAEMIA PATIENTS

Effect of infections on SCD

Children with sickle cell disease are 30–600 times more likely to develop invasive pneumococcal disease (IPD), including pneumonia, meningitis, and septicaemia. Overwhelming sepsis can develop rapidly with no obvious primary source of infection, resulting in shock, disseminated intravascular coagulation (DIC), adrenal haemorrhage, and death within 24 to 48 hours. Mortality can reach 35–50% from septicaemia and 10% in meningitis. This is because children with SCD have a functional hyposplenism or asplenia which results in failure to phagocytose encapsulated organisms namely Streptococcus pneumonia, Hemophilus influenza and Salmonella. Children with SCD must therefore be vaccinated against streptococcus pneumonia as well as be given penicillin prophylaxis to counter Streptococcus serotypes not covered by the vaccination. In addition, they must also be vaccinated against Hemophilus influenza type B and Neisseria meningitides.

Pneumococcal Vaccine

Pneumococcal vaccine is recommended for all sickle cell disease patients. There are currently 3 types of pneumococcal vaccines: pneumococcal conjugate vaccine (PCV10 or Synflorix), pneumococcal conjugate vaccine (PCV13 or Prevnar 13®) and pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax®). In Zambia currently, PCV 10 is the vaccine available under the Ministry of Health.

Pneumococcal conjugate vaccine

This vaccine induces an effective response in infants under 2 years, with an appropriate memory response after a booster dose. However, it covers 10 or 13 serotypes most of which cause infection in children less than 2 years of age but only 50% in adults.
In view of the difference in immunogenicity, polysaccharide conjugate vaccines are indicated in children less than 2 years of age whilst the pneumococcal vaccine can be given to ages 2 years to 65 years; in addition to the polysaccharide conjugate vaccine.

Pneumococcal Polysaccharide Vaccine

The Pneumococcal Polysaccharide (PPSV) vaccine (Pneumovax, PPS-23) consists of 23 purified antigens which should protect against 75% of invasive and respiratory infections. Polysaccharide vaccines however, neither provoke immunogenicity in children less than 2 years of age nor stimulates an adequate antibody response with immunological memory. Thus, a repeat exposure to the antigen does not produce a booster antibody response. It is therefore not very useful in children under 2 years of age. The effectiveness of the vaccine also diminishes over time. Thus, a booster is required every 5 years.

Meningococcal vaccine

There 13 serotypes of Neisseria meningitides of which A, B, and C cause 90% of disease. Nevertheless, W and Y have also now become more prevalent while serotype A is common in the sub-Saharan region of Africa. Five main types of vaccines against Neisseria meningitides have been developed.

Quadrivalent vaccines

There are 3 quadrivalent vaccines; 2 conjugate vaccine namely Menveo (MenACWY-CRM) and Menactra (MenACWY-D) and one polysaccharide vaccine namely Menomune. These all work against serotypes A, C, W and Y. Menveo is approved for children 2 months to 55 years of age. Menactra is not approved for children younger than 9 months but can be used up to 55 years of age. Menomune does not cause prolonged immunogenicity in children and therefore is not recommended for use in children. Menoveo is conjugated to Corynebacterium diphtheriae CRM_{197} protein while Menactra is conjugated the Corynebacterium diphtheriae toxoid and this increases immunogenicity of antibody production of up to 5 years). Menveo and Menactra cause increased antibody production with booster doses and herd immunity

Bivalent vaccine

Menhibrix is a bivalent vaccine working against meningococcal serotypes C and Y as well as Hemophilus influenza. It can be administered to children from 6 weeks of age to 18 months FDA approves new combination vaccine that protects children against two bacterial diseases.

Monovalent vaccines

Serotype A vaccine called MenAfriVac works against serotype A and has been used to contain outbreaks in sub-Saharan Africa. Serotype B vaccine works against only serotype B infection. It was difficult to produce but is now on the immunization schedule in Europe.

Menveo is being recommended for Sickle cell patients in Zambia for immunization against Meningococcal infection. It will however not cover all the serotypes but most of the common ones causing infection.

Recommended immunization schedule for SCD patients in Zambia

- Infants and Children younger than 2 Years of Age
- PCV10 or PCV 13 is recommended to be given routinely to infants as a series of 4 doses, one dose at each of these ages: 2 months, 4 months, 6 months, and 12 through 15 months.
- In Zambia, the routine child immunization schedule can be followed as follows for the first 3 doses: 6 weeks, 10 weeks and 14 weeks. The fourth dose must be given between 12 through to 15 months of age
- All 4 doses must be given to complete immunization.
- Children who miss their shots or start the series later should still get the vaccine. The number of doses recommended and the intervals between doses will depend on the child's age when vaccination begins.

- Children 2 through 5 Years of Age
- Children 24 months through 5 years of age with SCD should get 1 or 2 doses of PCV 10 or13 if they were not vaccinated or did not complete the 4 doses for pneumococci.

- Children 6 through 18 Years of Age
- A single dose of PCV10 or 13 should be given to children 6 through 18 years of age who have not previously received PCV 10 or13, regardless of whether they have previously received the 7-valent pneumococcal conjugate vaccine (PCV7) or the 23-valent pneumococcal polysaccharide vaccine (PPSV23).

Pneumococcal vaccination for adults with SCD

The pneumococcal polysaccharide vaccine (PPSV) that includes 23 serotypes, has been shown to be 50-85% effective in preventing invasive disease caused by those 23 serotypes in adults with healthy immune systems.

Therefore, immunization of adults against pneumococci also offers protection against pneumococcal invasive disease and pneumonia.

Indication for PPSV

Anyone 2 through 64 years of age with sickle cell disease must receive PPSV23. PPSV23 may be less effective for some people, especially those with lower resistance to infection. But these people should still be vaccinated because they are more likely to have serious complications if they get pneumococcal disease.

In Zambia, the following is recommended:

- Adults 19 years of age or older with SCD, and who have not previously received PCV10 or 13 must receive vaccination against pneumococci. They should get a dose of PCV10 or 13 first and should also continue to receive the recommended doses of PPSV23.
- Adults 19 years or older with sickle cell disease who have previously received one or more doses of PPSV23, should also receive a dose of PCV13 and should continue to receive the remaining recommended doses of PPSV23.
- The table below shows the current immunisation schedule for children in Zambia.

Table 12.1: Immunisation Schedule in Zambia

BCG (at birth). If no scar after 12 weeks, repeat dose. Unless symptomatic HIV.	
OPV 0 (at birth to 13 days)	
OPV 1 (at 6 weeks)	**DPT- HepB- Hib 1** (at 6 weeks)
OPV 2 (at least 4 weeks after OPV 1)	**DPT- HepB- Hib 2** (at least 4 weeks after DPT-HepB- Hib 1)
OPV 3 and **IPV** (at least 4 weeks after OPV 2)	**DPT- HepB- Hib 3** (at least 4 weeks after DPT-HepB- Hib 2)
OPV 4 (at months, only if OPV 0 was not given)	**Measles** (at months, or soon after. Unless symptomatic HIV)
PCV 1 (at 6 weeks)	**Measles** (at 18 months. Unless symptomatic HIV)
PCV 2 (at least 4 weeks after PCV 1)	**ROTA VACCINE 1** (at 6 weeks)
PCV 3 (at least 4 weeks after PCV 2)	**ROTA VACCINE 2** (at 4 weeks after ROTA 1)

Table 12.2: Additional Recommended Immunization Schedule for SCD

Age group	Pneumococcus	Meningococcus
Under 2 years	Routine vaccination together with other childhood vaccinations[a] **PCV 10** or 13 starting at 6 weeks, given every 4 weeks for 3 vaccinations, followed by the 4th dose between 12-15 months	**Menveo vaccine** Dose 1 at age 8 weeks: 4-dose series at 2, 4, 6, 12 months Dose 1 at age 7–23 months: 2-dose series (dose 2 at least 12 weeks after dose 1 and after age 12 months)
Age 2–5 years (fully immunized)	Single dose **PPV**	Administer booster dose 3 years after completion of primary vaccination and then subsequent booster doses every 5 years
Age 2–5 years (unvaccinated or partially vaccinated)	Two doses of **PCV 10** given 2 months apart, followed 2 months later by PPV	Dose 1 at age 24 months or older: give 2-dose series at least 8 weeks apart
Age >5 years (fully vaccinated)	Single dose **PPV**	Administer booster doses every 5 years.
Age >5 years (unvaccinated)	Single dose **PPV**	Children without a history of Meningitis vaccination should receive 2 primary doses of Menveo at least 8 weeks apart (administer at least 4 weeks after completion on PCV13 series)
Reinforcing immunization	**PPV** every 5 years	Administer Menveo booster doses every 5 years.

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CHAPTER 13: CURATIVE THERAPY

Haemopoietic stem cell transplant (HSCT) or Bone marrow transplant (BMT) can cure SCD. BMT involves the administration of healthy hematopoietic stem cells in patients with dysfunctional or depleted bone marrow. This helps to augment bone marrow function and allows to generate functional cells that can replace the dysfunctional ones in cases like sickle cell disease.

There is no global consensus on which patients should be offered BMT. Each treatment centre has its own indications and thresh holds for the procedure still vary. Thus, the risk-to-benefit ratio must be assessed carefully before the decision is made to have BMT. With the advent of cord blood stem cell transplantation and with the development of less immune-ablative conditioning regimens, perhaps BMT will gain wider acceptance and use. The lack of availability of a matched donor and the fact that the procedure is expensive limits the utility of BMT.

Currently BMT is unavailable in Zambia and few patients wishing to access the service, do so abroad, at their own expense, mainly in India. The demand for BMT is increasing and with collaboration, there are prospects that the service might be available locally in the near future. With this, it is important that guidelines are developed to provide guidance on which patients require BMT. With the coming of the new-born screening for SCD, it is envisaged that with early diagnosis, patients presenting early in infancy with severe forms of SCD become potential candidates for consideration for BMT.

Gene therapy is emerging as a possible cure for severe SCD. Experimental approaches include modification of autologous stem cells with lentiviral vectors to add normal globin genes, gene editing to correct the SCD mutation, and manipulations to enhance production of foetal haemoglobin. Successful results in individual patients has been reported in research settings, and clinical trials are in progress and their application remain experimental as at now.

Indications for Bone Marrow Transplant

Majority of published series reports and most paediatric haematologist agree that the following are indications for BMT in children:

- Stroke or silent cerebral infarction
- Recurrent acute chest syndrome or
- Frequent VOC despite hydroxyurea with good compliance

In adults, the following are the indications for BMT:

- Cerebrovascular disease
- Osteonecrosis
- Red cell alloimmunisation
- Recurrent acute chest syndrome
- Recurrent vaso- occlusive crisis despite hydroxyurea
- Elevated Tricuspid Regurgitant Jet velocity (TRJ)

For Zambia, with non-availability of this expensive procedure, the following indications can be considered:

1) Patients developing or already have end organ damage despite being on chronic/prophylactic blood transfusion and/or maximal dose of disease modifying therapy such as hydroxyurea and regular follow up
2) Patients with silent and overt stroke since they tend to recur
3) Patient with iron overload and cannot continue chronic transfusion and/or cannot afford chelating therapy
4) Recurrent severe forms of VOC, despite being on prophylactic/chronic blood transfusion and/or maximal dose of disease modifying therapy such as hydroxyurea and regular follow up: ACS, Priapism

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CHAPTER 14: GENETIC COUNSELLING

Sickle cell trait (SCT) is not considered to be a health problem, but individuals who test positive should be informed about the implications for their health and family planning. Thus, the primary issues addressed in this chapter are what information should individuals receive, and who should provide it.

Most individuals with SCT may not recall or understand the implications of having the SCT by the time they reach childbearing age. Currently, there are two major circumstances in which adults will learn that they have SCT, leading to two groups of counselees:

1. Parents of a child with SCT. When a new-born with SCT is identified through screening, at least one of the parents will
have SCT.

2. Pregnant women. During prenatal care, women from racial groups with a high prevalence of the sickle cell gene frequently are tested for the gene.

SCT counselling has two components—

- **Education**: that is, to enable individuals to make informed decisions, in their own interest, about future family planning.
- **Decision-making** with the focus being on education and informed decisions, in their best interest, about the current pregnancy.

Note: *An essential principle for each counselling group is that advice, personal opinions, and societal positions must not be given or implied. This admonition must be obeyed strictly because, in each case, self-determination is the desired outcome. Counsellors must not influence decisions inappropriately—overtly through statements or covertly through facial expressions, tone of voice, body language, etc.—particularly if asked, "What should I do?"*

Basic content for all sessions

- Purpose and goal of the session
- How sickle cell conditions are acquired—genetic basis
- Difference between SCT and SCD
- Health problems that can occur in SCD
- Variability of and inability to predict occurrence and frequency of health problems in SCD
- Potential outcome of each pregnancy if one or both partners has SCT
- Family planning options
- Racial groups who have SCD and the percent of individuals in the counselee's racial group who have SCT and SCD
- Average life span of individuals with SCT and SCD

Additional content for pregnancy outcome decision making sessions

There are several noncognitive factors that pregnant women (and the fathers) may wish
to consider in order to reach a decision consistent with the goal. These factors include:

- Coping skills relative to a child with a serious illness
- Personal and cultural values relative to childbearing
- Religious beliefs
- The need and desire to have children
- Feelings and attitudes about abortion
- Belief about self-determination versus fate as determinants of adverse events

Instructional/educational techniques

- Use lay language whenever possible

- Translate scientific terms into common everyday usage whenever possible.
- Use graphics to illustrate key points.
- Establish a dialogue rather than using a strict lecture format or information giving format.
- Implement a pre- and post-assessment.
- Use the post-assessment as an opportunity to clarify misinterpretation or uncertainty that the genetic test revealed.
- Provide literature written in lay language covering the essential facts.
- Make available sources of more detailed information for those who are interested.
- Communicate the availability of the provider for follow-up questions.
- Follow a structured protocol to ensure that the essential features are covered, but
- This should not prevent interaction.

Minimal acceptable achievements

This is minimal acceptable achievement level in a basic counselling session. For example, the counselee should understand:

- The family planning options open to persons with SCT.
- SCT is not an illness, so no restrictions need to be placed on his or her activities.
- The variability in severity of SCD.
- Both parents must have the trait for the child to have SCD.
- The 25 percent chance that each pregnancy will result in a child with SCD if both parents have the trait.
- Some of the reasons couples might decide to have or not have children if both have the trait.

Extracted from:

1) **The management of Sickle Cell Disease.** *NIH Division of blood diseases and resources. 2014.*

CHAPTER 14: PALLIATIVE CARE IN SICKLE CELL DISEASE

Global context

The provision of palliative and end-of-life care for patients with progressive disease is inadequate in almost every country in the world. It is estimated by the WHO that annually over 40 million people worldwide could benefit from palliative care (PC) services. The large majority (78%) of these people live in low- and middle-income countries, and the need is rapidly increasing due to rising rates of non-communicable diseases (NCDs) (WHO, 2018).

Zambia context

Historically, PC in Zambia was primarily propagated through the HIV/AIDS epidemic by NGOs, FBOs, and CBOs. PC services were provided by hospices, where ill people were nursed in an effort to provide a more comfortable and manageable environment in the last few hours, days, or weeks of their lives. Like other sub-Saharan African countries, Zambia has experienced a shift towards increasing numbers of NCDs; HIV and other infectious disease rates remain high; Zambia's responsibility to care for the aging and dying will only become more substantial with time. Currently PC services do exist, but they are disjointed; The Cancer Diseases Hospital (CDH) in Lusaka, and the Livingstone Central Hospital (LCH) in Livingstone are the only institutions with functional PC teams.

Definition of palliative care

Palliative care is defined as an "approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (WHO 2002). Palliative care therefore provides comprehensive care for people living with life-threatening illnesses and starts from diagnosis, continues throughout the disease trajectory, and provides bereavement support after death. It incorporates the principles of hospice care, provides supportive care and supports patients and families at the end of life.

Principles

The provision of palliative care will be guided by the following key principles:

- Providing care to clients as close to family as possible by primary and secondary caregivers.
- Ensuring standard quality care.
- Protecting and upholding the interests and rights of both care providers and recipients of palliative care services.
- Ensuring continued monitoring and evaluation of palliative care services.
- Ensuring that palliative care is integrated into the healthcare system.
- Ongoing training for palliative care providers with particular emphasis on pain and other symptom control including adherence support for those already on treatment.

Goal of Palliative Care

The goal is to improve the quality of life for individuals who are suffering from severe diseases.

Components of palliative care patient support services

Three categories of support:

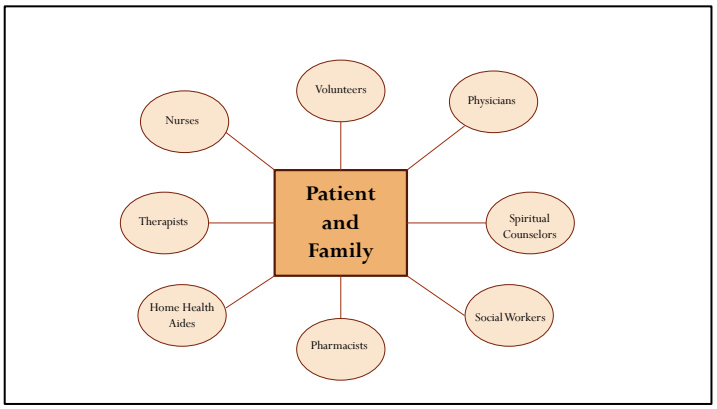
1. **Pain management** is vital for comfort and to reduce patients' distress. Health care professionals and families can collaborate to identify the sources of pain and relieve them with drugs and other forms of therapy.
2. **Symptom management** involves treating symptoms other than pain such as nausea, weakness, bowel and bladder problems, mental confusion, fatigue, and difficulty breathing
3. **Emotional and spiritual support** is important for both the patient and family in dealing with the emotional demands of critical illness.

Who provides palliative care?

Usually provided by a team of individuals:

- Interdisciplinary group of professionals
- Team includes experts in multiple fields:
- Doctors
- Nurses
- social workers
- massage therapists
- Pharmacists
- Nutritionists

Fig 14: Team of palliative care



Illustrate from palliative training material

Benefits of palliative care to the patient

- Helps patients gain the strength and peace of mind to carry on with daily life
- Aid the ability to tolerate medical treatments
- Helps patients to better understand their choices for care

Benefits of palliative care to the family

- Helps families understand the choices available for care
- Improves everyday life of patient, reducing the concern of loved ones
- Allows for a valuable support system

Conclusion

Palliative care is a necessary service which must be integrated in the treatment and management of Sickle cell Disease, as it is not only medical but must be managed holistically

Reference

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CHAPTER 15: SICKLE CELL DISEASE RESEARCH

There are a lot of opportunities for sickle cell disease research in Zambia. Some of the present gaps in knowledge include

- Burden of SCD in the country (Prevalence/Incidence)
- Epidemiology and demographics of SCD in Zambia
- Life expectancy, morbidity and mortality in SCD
- Genomics of SCD in Zambia
- Service delivery for persons with SCD in Zambia
- Management options and interventions for SCD

Earlier published research on SCD in Zambia

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Some most recent research in SCD done in Zambia include

1) Taonga Musonda, Mildred Zulu, Mulemba Samutela et al: **Leucocytosis and Asymptomatic Urinary Tract Infections in Sickle Cell Patients at a Tertiary Hospital in Zambia**. *Anaemia* 2020 https://doi.org/10.1155/2020/3792728
2) RM Musowoya, P Kaonga, A Bwanga et al. **Predictors of musculoskeletal manifestations in paediatric patients in presenting with sickle cell disease at a tertiary hospital in Lusaka, Zambia.** *Bone Joint Open* 2020; 1-6: 175-181
3) Chunda-Liyoka, A. A. Kumar, P. Sambo et al: **Application of a public health strategy to large-scale point-of-care screening for sickle cell disease in rural sub-Saharan Africa.** *Blood Advances* 2018 2:1-3; doi: https://doi.org/10.1182/
4) D Sinkala, L.C. Fleming, F Silwimba, K.H. Jacobsen: **Health services access for young children with sickle cell anaemia in the Chilubi district of Zambia**. *Medical journal of Zambia* 45(3):134-138 · July 2018.
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6) Kumar AA and Chunda-Liyoka et al**: From the Bench to the Field in Low-Cost Diagnostics**. *Angew chem. Int. Ed. 2015, 54,5836 –5856*
7) Kumar AA, and Chunda-Liyoka C et al: **Evaluation of a density-based rapid diagnostic test for sickle cell disease in a clinical setting in Zambia**. *PLoS One.* 2014 Dec 9; 9(12).

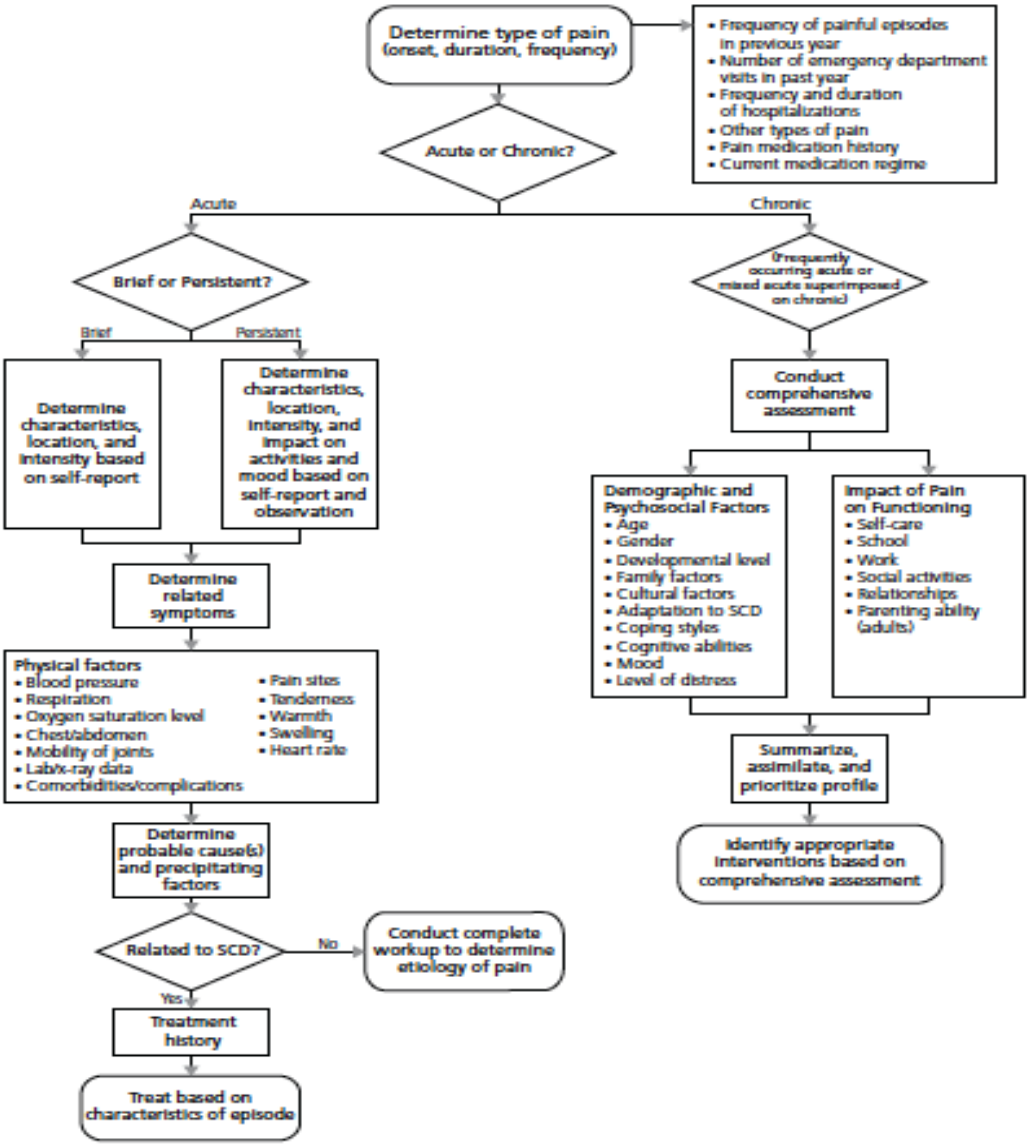
Studies conducted by Post-graduate students from the cohort of SCD patients at the UTHs include

- Prevalence of Hepatitis B and C in Sickle cell Disease Patients at University Teaching Hospital, Lusaka, Zambia
- Indications for blood transfusion and usage of blood products at a tertiary hospital in the paediatric medical ward at the University Teaching Hospital, Lusaka, Zambia.
- Iron deficiency in SCD patients
- Ocular manifestations of SCD patients
- Prevalence and risk factors of chronic kidney disease in steady state sickle cell anaemia patients aged 5 to 16 years at the University Teaching Hospital, Lusaka, Zambia.

APPENDICES

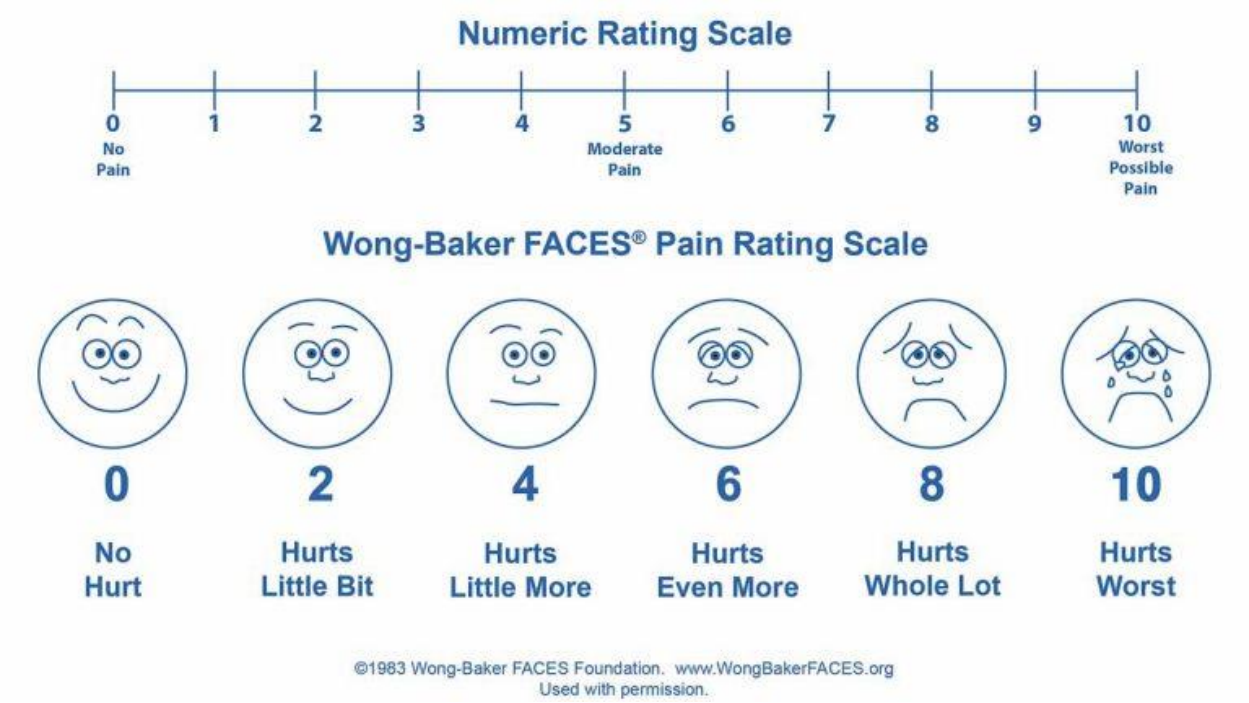
Appendix 1: Evaluation of pain in a person with SCD

Evaluation of a SCD patient presenting with pain



Extract from NIH-NHLB 'The management of SCD"

Wong-Baker Faces Pain rating scale in paediatric patients



Pain assessment in adolescents and adults

For adolescents and adults, the card is folded along the broken line so that each measure is presented separately in the numbered order.

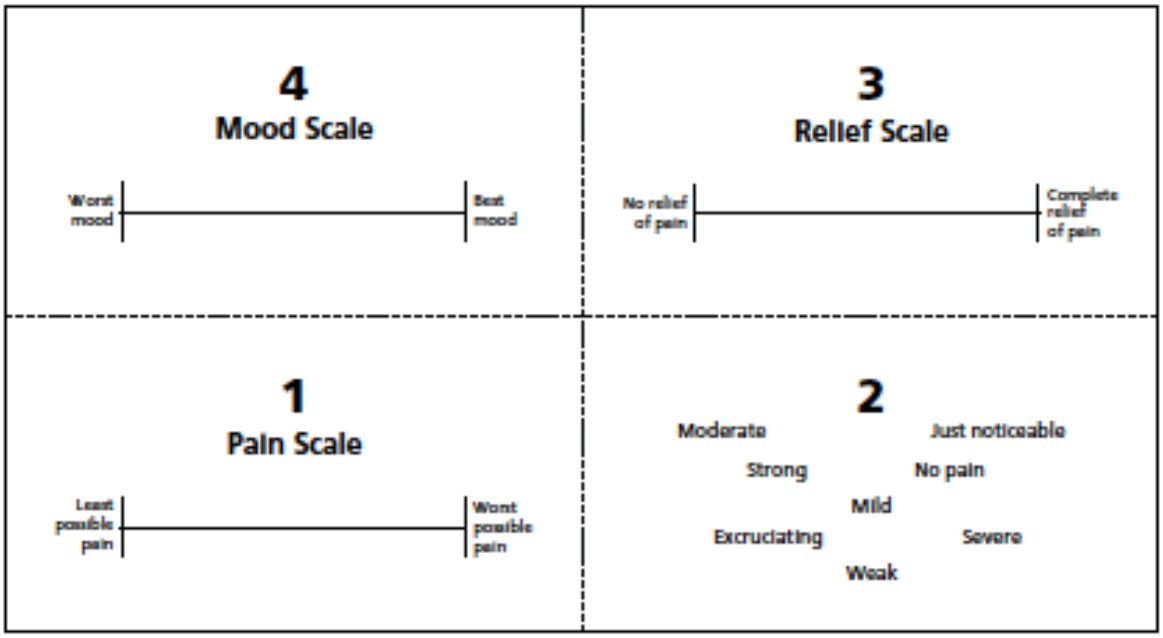


Figure 4. Multidimensional Assessment of Acute Pain

DATE ___/___/_____ TIME ___:___

1. Circle the number that describes your pain right now.

0 1 2 3 4 5 6 7 8 9 10

No pain — Worst possible pain

2. Circle the number that describes your pain relief.

0 1 2 3 4 5 6 7 8 9 10

No relief — Complete relief

3. Circle the number that best describes your mood.

0 1 2 3 4 5 6 7 8 9 10

Worst mood — Best mood

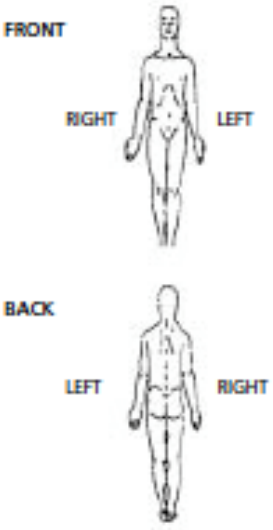
4. Circle the number that describes how drowsy you feel.

0 1 2 3 4 5 6 7 8 9 10

Not drowsy — Asleep

5. Shade the figure where you feel pain.

6. Mark an X where you hurt most.



Extract from NIH-NHLB 'The management of SCD"

Appendix 2: UTH Children's Hospital hyper-transfusion protocol

UNIVERSITY TEACHING HOSPITAL- CHILDREN'S HOSPITAL HYPER-TRANSFUSION PROTOCOL IN SICKLE CELL DISEASE

NAME: ……..

AGE: ……. SEX: ……. BLOOD GROUP: …….

FILE NUMBER: ……

TRANSFUSE PACKED RED CELLS AT 10 mL/Kg

INDICATION……

MONTH 1

WEEKLY TRANSFUSIONS (X4)

NUMBER	DATE TRANSFUSED	MOs SIGNATURE
1		
2		
3		
4		

MONTHS 2 AND 3

BIWEEKLY BLOOD TRANSFUSIONS (X4)

NUMBER	DATE TRANSFUSED	MOs SIGNATURE
5		
6		
7		
8		

MONTHS 4 – 6

MONTHLY BLOOD TRANSFUSIONS (X3)

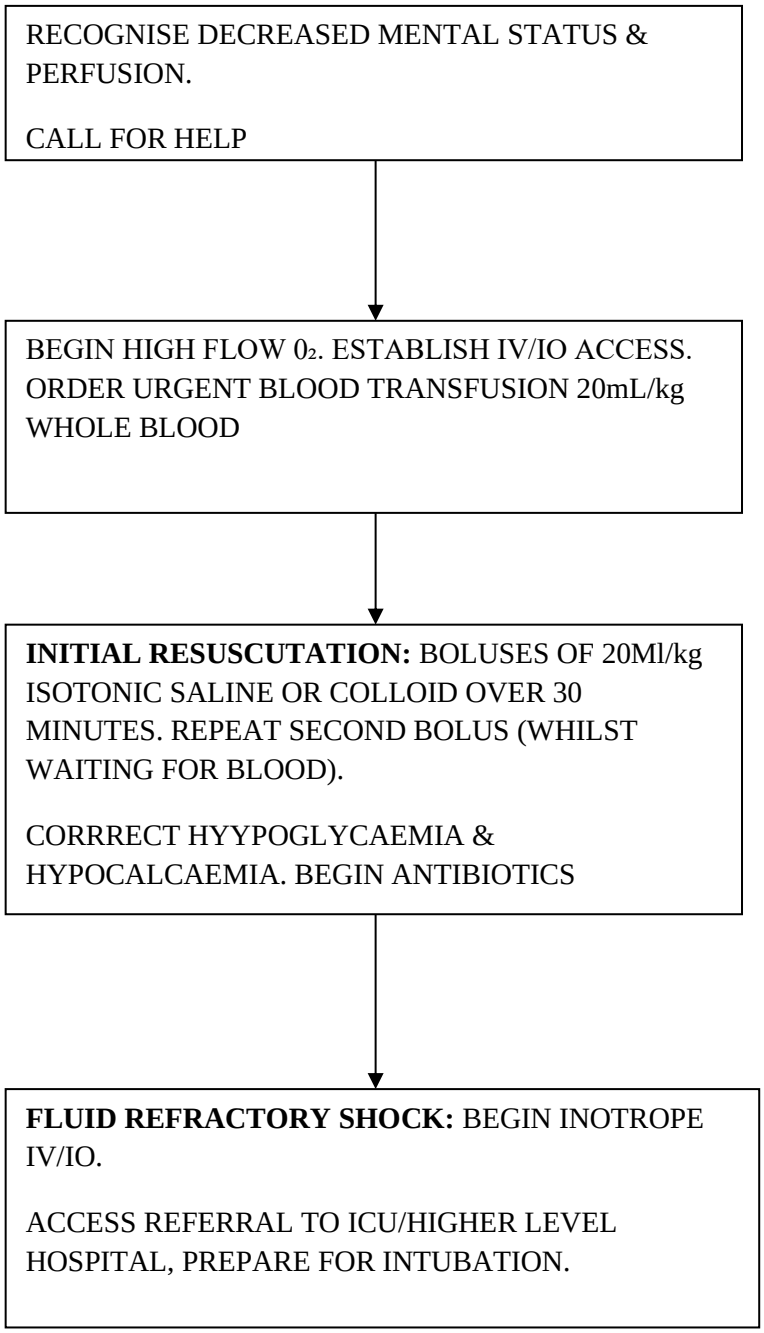
NUMBER	DATE TRANSFUSED	MOs SIGNATURE
9		
10		
11		

Date Started: ……

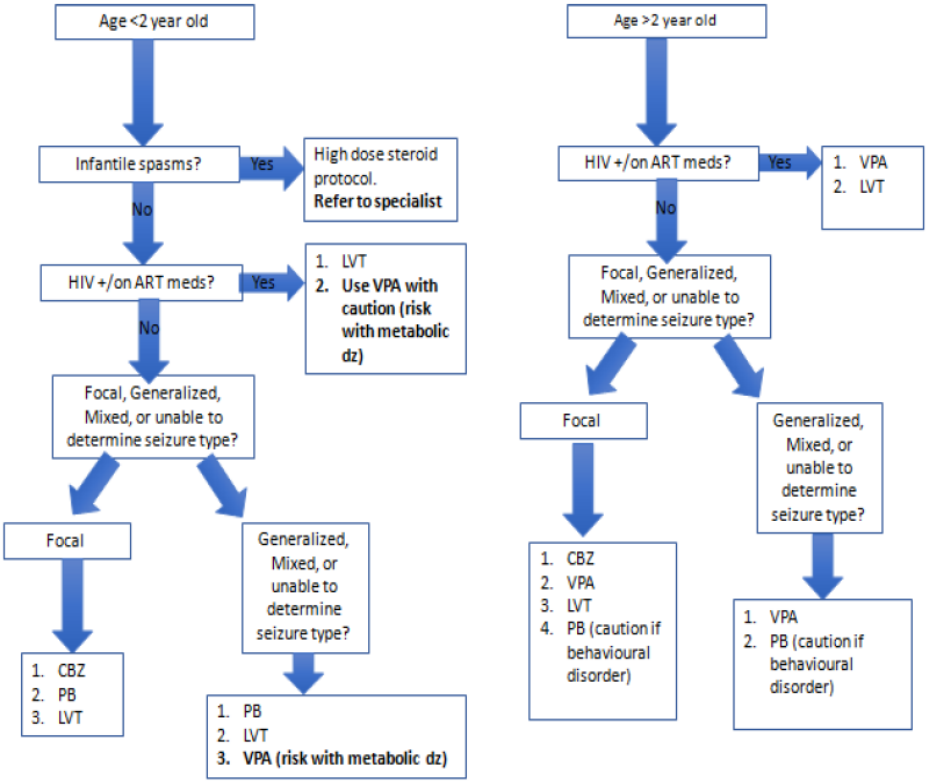
Date Completed: ……

Appendix 3: Management of Shock

STEPWISE MANAGEMENT OF SHOCK

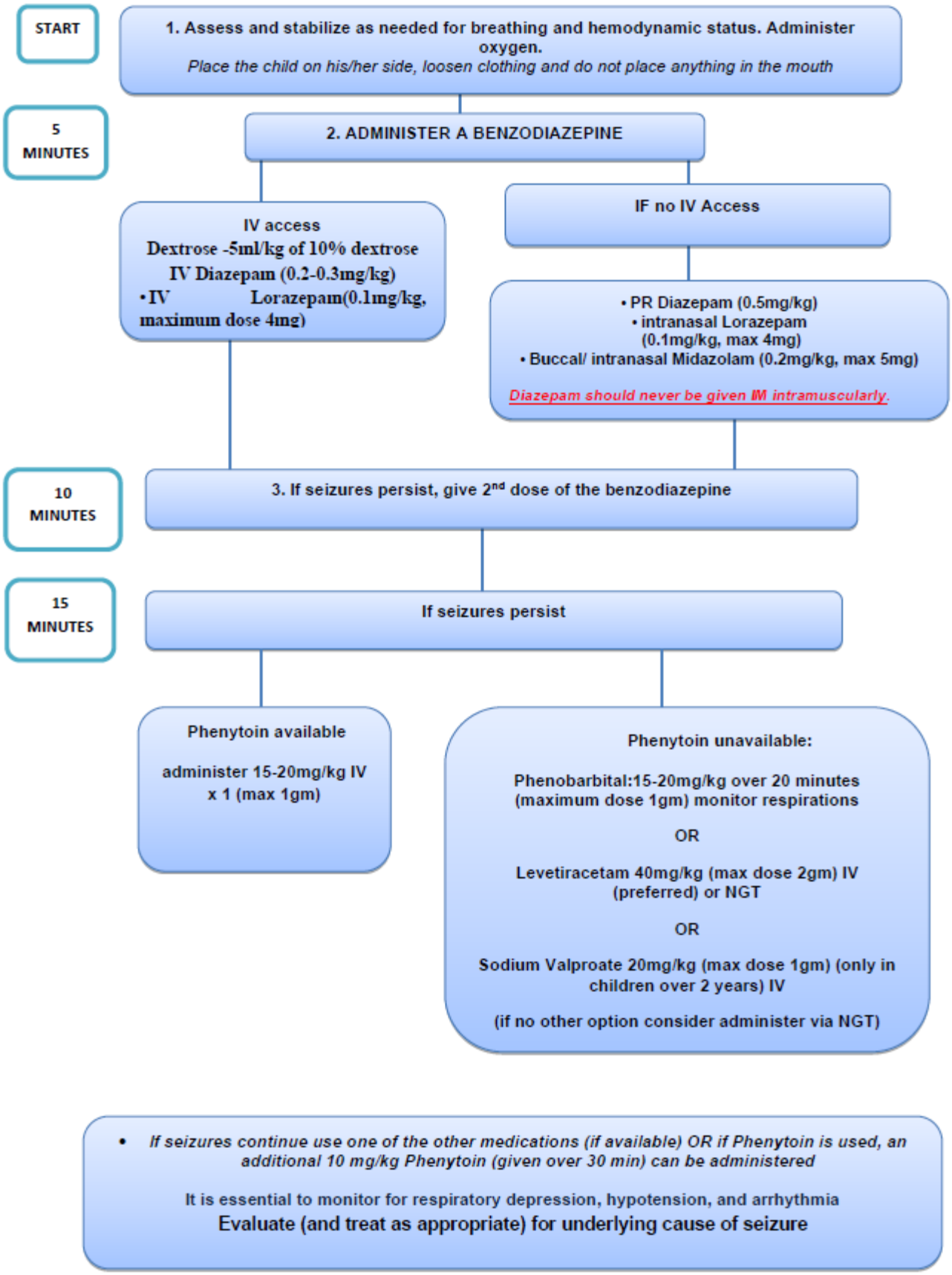


Appendix 4: AED selection



CBZ: Carbamazepine, PB: Phenobarbitone, LVT: Levetiracetam, VPA: Valproic Acid (Sodium Valproate)

Appendix 5: Management of status epilepticus



- *If seizures continue use one of the other medications (if available) OR if Phenytoin is used, an additional 10 mg/kg Phenytoin (given over 30 min) can be administered*

It is essential to monitor for respiratory depression, hypotension, and arrhythmia

Evaluate (and treat as appropriate) for underlying cause of seizure

Appendix 6: UTH Children's Hospital Transition form

REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH

UTH CHILDREN'S HOSPITAL

Medical Summary and Transition Form

Date Completed:	Date Revised:
Form Completed By:	
Contact Information	
Name:	Nickname:
DOB:	Preferred Language:
Parent (Caregiver):	Relationship:
Address:	
Cell #: Home #:	Best Time to Reach:
E-Mail:	Best Way to Reach: Text Phone Email
Health Insurance/Plan:	Group and ID #:
Emergency Care Plan	
Emergency Contact: Relationship:	Phone:
Preferred Emergency Care Location:	

Diagnoses and Current Problems	
Problem	Details and Recommendations
☐ Primary Diagnosis	
☐ Secondary Diagnosis	
☐ CNS	
☐ Renal	
☐ Cardiovascular	
☐ Orthopaedic/Musculoskeletal	
☐ Physical Anomalies	
☐ Respiratory	
☐ GIT	
☐ Other	

Medications

Medications	Dose	Frequency	Medications	Dose	Frequency

Health Care Providers

Provider	Primary and Specialty	Clinic or Hospital	Phone	Fax

Prior Surgeries, Procedures, and Hospitalizations					
Date					
Date					
Date					
Date					
Date					
Baseline					
Baseline Vital Signs:	Ht	Wt	RR	HR	BP
Baseline Neurological Status:					

Most Recent Labs and Radiology		
Test	Date	Result
EEG		
EKG		
X-Ray		
C-Spine		
MRI/CT		
Other		
Other		

Special Information that the patient wants health care professional to know

Patient signature Date	Print Name	Phone Number
Parent/Caregiver Date	Print Name	Phone Number
Primary Care Provider Signature Date	Print Name	Phone Number
Care Coordinator Signature Date	Print Name	Phone Number

Appendix 7: Sickle Cell Disease Follow Up Card

MINISTRY OF HEALTH

SICKLE CELL DISEASE FOLLOW-UP CARD

STATION:

CARD NUMBER:

1. PATIENT'S PARTICULARS

First Name:	**Surname:**	**Sex: M/F**
DOB:	**Residential Address:**	
Mobile phone #:	**Email address:**	
Hospital File #:		

2. NEXT OF KIN PARTICULARS

First Name:	**Surname:**
Residential Address:	**Mobile phone #:**
Relationship: Father □ Mother □ Sibling □ Spouse □ Other □	

3. DIAGNOSIS DETAILS

□ Clinical:	**Date:**	**Place:**
□ Sickling test:	**Date:**	**Place:**
□ Hb Electrophoresis:	**Date:**	**Place:**

□ **Hb Solubility Test:**	**Date:**	**Place:**
□ **HPLC:**	**Date:**	**Place:**

4. DRUGS & VACCINES

□ **Penicillin Prophylaxis:**	**Dose:**	**Start Date:**
□ **Folic Acid:**	**Dose:**	**Start Date:**
□ **Hydroxyurea:**	**Dose:**	**Start Date:**
□ **Daraprim:**	**Dose**	**Start Date:**
□ **Others:**		**Start Date:**
□ **Pneumococcal vaccine:**		**Date:**
□ **Others:**		**Date:**

5. APPOINTMENTS

Date	Weight	Height/Length	Hb	MO/ Nurse