Sickle Cell Disease: Paediatrics

Document Control:

For Use In:	Paediatrics, CAU, Buxton, ChED		
	NNUH		
Search Keywords	Sickle, sickle cell, SCD		
Document Author:	Jo Ponnampalam		
Document Owner:	Paediatric Haematology		
Approved By:	Clinical Guidelines Assessment Panel		
Ratified By:	Clinical Safety Effectiveness and Sub-Board		
Approval Date:	7th December 2024	**Date to be reviewed by:** This document remains current after this date but will be under review	7th December 2025
Implementation Date:	N/A		
Reference Number:	1308		

Version History:

Version	Date	Author	Reason/Change
V1.0	December 2011	Consultant Paediatrician	To originate document
V4.0	December 2024	Consultant Paediatrician	Adapted from regional guidance
V5.0			

Previous Titles for this Document:

Previous Title/Amalgamated Titles	Date Revised
Sickle Cell Guidelines (Paediatrics)	December 2024

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:

This guideline has been extracted for use from CUH (Specialist Haemoglobinopathy Team, SHT) to be used within the Jenny Lind Children's Hospital (Local Haemoglobinopathy Team, LHT), which is part of the Regional Haemoglobinopathy Network
Paediatric Medical Consultants NNUHFT
Dr Hamish Lyall, Consultant Haematologist, NNUHFT
Dr Suzanne Docherty, Consultant Haematologist, NNUHFT

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g., changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is clinical guideline applicable to NNUH; please refer to local Trust's procedural documents for further guidance, as noted in Section 4.

For any non urgent queries, please email the Paediatric Haematology secretary within the JLCH paedoncadmin@nnuh.nhs.uk

Sickle Cell Disease: Paediatrics

Contents Page

Sickle Cell Disease: Paediatrics

1. Introduction

1.1. Rationale

Sickle cell disease (SCD) describes an inherited disorder of haemoglobin, where reduced oxygenation or dehydration leads to red cell shape change and microvascular sequestration of erythrocytes causing pain and organ damage.

Factors which can precipitate a crisis include:

- Infection (fever)
- Exposure to cold
- Dehydration
- Deoxygenation
- Strenuous exercise
- Emotional stress
- Menstruation
- Pregnancy

The majority of painful crises are associated with aches and pains in the bones and joints, but when a sickle crisis affects an organ, it is considered a haematological emergency. Due to impaired splenic function patients with sickle cell disease are prone to infections, particularly pneumococcus, and should therefore be on prophylactic penicillin and have additional vaccinations (see table appendix 3)

The majority of patients will present with a known sickle cell disorder diagnosis picked up on newborn screening (Guthrie test) and confirmed by liquid sample for haemoglobin electrophoresis (The paediatric haematology nurse will have this form and address for laboratory if sample requires sending).

A diagnosis of sickle cell disease can be confirmed on blood film, sickle screen, and followed by haemoglobin electropheresis. To confirm the diagnosis out of hours a blood film and sickle screen should provide sufficient diagnostic certainty and allow initiation of treatment for a painful crisis or other emergency as outlined in the BCSH guidelines.

1.2. Objective

Children with Sickle Cell Disease can have crises in their condition which require hospital admission. These crises occur with varying frequency and severity. It is important to recognise that patients often deal with crises at home so when they present to hospital in an acute crises these patients can be very ill and in severe pain.

The objective of the guideline is to:

- Ensure prompt assessment and administration of appropriate analgesia within 30 minutes

1.3. Scope

Paediatric Haematology, for the care of children with sickle cell disorders, covering the diagnosis and management of sickle-related complications

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
ABG	arterial blood gases
CNS	central nervous system
CPAP	continuous positive airway pressure
CRP	C-Reactive protein
CT	computed tomography
CVA	cerebral vascular event
CXR	chest x-ray
EEG	electroencephalogram
ESR	erythrocyte sedimentation rate
FBC	full blood count
Hb	haemoglobin
HbSS	haemoglobin SS
IV	intravenous
LD	lactate dehydrogenase
LFT	liver function test
MRI	magnetic resonance imaging
MSU	mid-stream urine
NCA	Nurse controlled analgesia
NMH CNS	Non-malignant haematology clinical nurse specialist
PCA	Patient controlled analgesia
PCV	packed cell volume
PRN	as required
SCD	sickle cell disease
TCD	Transcranial doppler scan
TIA	transient ischaemic attack
U+Es	urea and electrolytes
UTI	urinary tract infection

2. Responsibilities

It is the responsibility of all staff involved in caring with Children and young people with Sickle Cell disease to be aware of this guideline, and follow accordingly.

Children with sickle cell disease will be admitted under Dr Jo Ponnampalam, Consultant Paediatrician, as named consultant.

Please inform Dr Ponnampalam of any sickle cell admissions to the JL Children's Hospital via email; in her absence or out of hours including weekends, please discuss all admissions with the Paediatric Haematology team at CUH(please contact via the Paediatric Oncology route) via the Addenbrookes switchboard.

3. Processes to be followed

3.1. History and Examination

3.1.1. Clinical assessment

A full history and examination must be carried out; remember that the parent knows the child better than we do. How ill is the child? Is this incident different / worse than usual?

Remember that patients can get dangerously ill very quickly, e.g. Pneumococcal infection and Chest syndrome. Pay particular attention to symptoms/signs of life-threatening complications including acute chest syndrome, septicaemia, splenic sequestration or aplastic crisis.

Note:
Extreme pallor, weakness, lethargy, breathlessness, headaches, fits, and priapism require urgent attention.

History taking must include:

- The site and intensity of the pain
- Any analgesia already taken
- Any focus of infection (including the urinary tract)
- Chest symptoms and signs, including respiratory rate, O2 saturations in air
- Any new neurological symptoms or signs
- Liver and spleen size (cm)
- Degree of pallor, blood pressure
- Ask about whether the child is taking regular prophylactic penicillin
- Any recent blood transfusion

NB: Children with HbSS can be jaundiced, anaemic and have a cardiac flow murmur normally.

3.1.2. Conditions requiring immediate admission

- Severe pain, or pain unresponsive to simple oral analgesia at home (i.e. requiring parenteral opiate analgesia)
- Increased pallor, breathlessness, exhaustion
- Marked pyrexia (> 38°C), tachycardia or tachypnoea, hypotension
- Chest pain; signs of lung consolidation
- Abdominal pain or distension, diarrhoea, vomiting
- Severe thoracic/back pain
- Headache, drowsiness, CVA, TIA, seizure or any abnormal CNS signs
- Priapism (> 4 hours, or stuttering)

- Hypoxia (O2 Saturation less than 95% in air)

3.1.3. Routine Investigations (all cases)

Blood Tests:

- FBC + reticulocytes
- Group, screen and save
- Hb electrophoresis
- Urea & electrolytes
- Creatinine
- LFTs, LDH
- CRP (maybe raised in vaso-occlusive crisis)

Microbiological screen:

- Urine dipstick & MSU culture
- Other tests:
- Pulse oximetry (SaO2) on air

In addition:

IF the patient has a fever: (see section 3.2.4)

Blood Culture MSU

Throat swab

Stool culture, if relevant (NB. Patients on Desferrioxamine, admitted with diarrhoea/abdominal pain, should have blood and stool screened for Yersinia and mucormycosis infections, and the DFO stopped).

IF breathless, respiratory distress, chest signs or low O2 saturation: (see section 3.4.1)

CXR

3.1.4. Additional Investigations

Certain tests are carried out if indicated, as follows:

Test	Indication
Blood Gases	If deteriorating O_2 sats in air
Serum amylase Abdominal ultrasound	Abdominal symptoms/signs Symptoms suggestive of cholecystitis

Screen stool for *Yersinia and mucormycosis*. Serum for *Yersinia* antibodies	Patients on desferrioxamine (DFO) with diarrhoea/abdominal pain (STOP DFO)
Parvovirus IgM serology	Fall in Hb with low retics
MRI scan of head	See stroke and other CNS complications
X-rays of painful joints/limbs*	Generally not helpful. See below
ECG	If possible arrhythmia or cardiac pain
Throat, nose, sputum, stool, wound, CSF cultures etc	As clinically indicated

* X-rays of bones and joints show little or no change in the first week of an acute illness and rarely differentiate between infarction and infection.

New patients to the hospital require the following routine investigations (there are usually carried out in the outpatient clinic unless initial presentation to the hospital is through ED)

Additional First Presentation Blood Tests

- Hb electrophoresis, including %HbF
- Extended red cell phenotype
- G6PD
- Ferritin
- Hepatitis B and C serology
- Parvovirus serology
- Consider HIV serology, particularly if transfused outside of UK

3.2. Painful Sickle Cell crisis: management

Management is supportive unless there are indications for exchange transfusion, which should first be discussed with the Paediatric Haematology/Oncology Consultant on call.

General management includes:

- Giving reassurance that the patient's pain will be relieved as soon as possible;
- Warmth; and establishing a position of maximum comfort
- Analgesia
- Hydration
- Regular observations and reassessment

If necessary;

- Establish i.v. access as soon as possible
- Identification and treatment of infection

NB-Oxygen is not routinely administered in painful crisis unless oxygen saturations are <95% in AIR. This is to prevent masking of an impending chest crisis, which is a medical emergency, and requires transfer to PICU for an exchange transfusion.

3.2.1. Analgesia

Pain in SCD may be severe and is often underestimated by medical and nursing staff.

Many children at presentation will already have been taking paracetamol and NSAIDs at home and therefore may need opiate therapy

An analgesic ladder is used according to the severity of pain – for assessment scoring of pain.

Prescribing guidelines in Paediatric Sickle Cell Pain Appendix 1

NB: All children receiving opiates will become **constipated**-consider adding laxatives when prescribing opioids

See **section 3.3** for other medications required.

3.2.2. Fluid replacement

Dehydration occurs readily in children with sickle cell disease due to impairment of renal concentrating power (hyposthenuria). Continued fluid loss without adequate replacement causes a reduction in plasma volume with an increased blood viscosity and aggravation of sickling.

Diarrhoea and vomiting are therefore of particular concern.

The ill child should be assessed for the degree of dehydration by

- The history
- The duration of the illness
- By clinical examination
- (if known) weight loss.

Hb and PCV (Hct) may be elevated as compared with the child's steady state values.

A fluid chart should be started and fluid balance monitored strictly, both input and output.

NB:

- Children with sickle cell disease need individualised fluid regimes which are regularly reviewed. They are often dry and will need additional fluids; conversely over-zealous fluid replacement may make the situation worse by precipitating cardiac failure and acute chest syndrome
- The oral route should be used whenever possible but children with severe pain who are not settling, or who have abdominal symptoms should receive intravenous re-hydration.
- Intravenous therapy should be stopped once the patient is stable and pain is controlled.

Fluids may be given orally or intravenously as described above. If IV re- hydration is required use standard fluid maintenance 0.9% Saline +/- dextrose and review the need for potassium.

Electrolytes should be reviewed, remembering that a slightly raised urea will be significant as these children normally have a low blood urea. Check U&Es at least daily and add KCl as required

3.2.3. Oxygen

The patient's oxygen saturation (SaO2) **should be monitored by pulse oximetry with regular readings in air (minimum 4 hourly).**

NB – it is vital oximetry is monitored IN AIR, as the measured saturation with supplemental oxygen may be falsely reassuring, and mask underlying worsening hypoxia.

- If SaO2 < 95% on air, give O2 by face mask. In any patient who is hypoxic consider sickle chest syndrome (see section 9): discuss with consultant on call if any concerns.
- Consider arterial gases if SaO2 on air is <90% or falling.

Remember that excess opiate analgesia can cause respiratory suppression (Naloxone should be prescribed PRN).

3.2.4. Fever and Infection

Pneumococcus is the most dangerous infection for a child with sickle cell disease but they are also susceptible to Haemophilus influenza, Meningococcus, Staphylococcus and Salmonella.

BEWARE: Children should have had Prevenar and Pneumovax (and also HIB) and be on prophylactic Penicillin

NB There can be poor adherence with oral antibiotic prophylaxis at home.

Always look for the focus of infection (blood, lungs, urine, and stool) and treat as appropriate.

Collect respiratory screen and covid swabs if appropriate.

Collect blood cultures, urine, and throat swabs starting antibiotics (but if the child is unwell or cannot pass urine, do not wait for specimen before starting on antibiotics. Document the reason).

- In uncomplicated painful crisis without specific evidence of infection increase prophylactic penicillin V to qds after cultures (blood, urine and any other source that is indicated) have been taken. If allergic to penicillin, use erythromycin qds.

3.2.5. All Children with Pyrexia

- Ceftriaxone IV
- Suggested antibiotic regimens (NICE Summary of antimicrobial prescribing guidance – managing common infections Dec 2018)
- BSH Guidelines (2015)

*If **chest crisis** is suspected, please contact CUH Paediatric Haematology team ASAP as this is a **medical emergency** and would require HDU/PICU care and consideration for X-change transfusion which is done at CUH for children(refer to Section 3.4.1 below)*

If true penicillin anaphylaxis, allergy seek microbiology advice.

This is a recommendation only and should be discussed with the local microbiology team, taking local antibiotic resistance profiles into consideration. See British Journal of Haematology, 2015,169,492–505

Metronidazole is not necessary for abdominal pain. If there is a suspected chest infection give IV Ceftriaxone. Reassess at 48 hours; if child well and cultures negative, could stop or change to oral.

Patients on desferrioxamine (DFO) who have diarrhoea should be started on ciprofloxacin immediately and the DFO stopped. Ciprofloxacin can be stopped when Yersinia infection has been excluded. Cases of salmonella should be discussed with the Infection control team.

3.3. Other Medication to be considered

Please write up for:

a) Folic acid

From	To	Dose
0	11 months	500 micrograms/kg (max 5mg) OD
≥1 year		5 mg od

b) Anti-emetic (if receiving opiate analgesia)
Cyclizine

From	To	Dose
6 years	12 years	25 mg tds
over 12 years		50 mg tds

Ondansetron

From	To	Dose
All ages		0.1mg/kg IV/PO (max 4mg) every 8 hours

c) Laxatives if receiving opiate analgesia (unless there are abdominal signs)
Lactulose

From	To	Dose (starting from)
1 month	11 months	2.5 mL BD
1 year	4 years	5 mL BD
5 years	10 years	10 mL BD
over 12 years		15 mL BD

Or Movicol Paediatric (if <12yrs), or Adult if ≥12yrs 1 sachet 1-2 times daily

d) Antipruritic (if receiving opiate analgesia)

Chlorphenamine (oral doses)

From	To	Dose
1 month	23 months	1 mg BD
2 years	5 years	1mg every 4-6 hours
6 years	11 years	2 every 4-6 hours
12 years and over		4 mg Every 4-6 hours

3.4. Potential life-threatening complications

3.4.1. Acute Chest Syndrome-

CUH must be contacted urgently and discuss transfer of child; duty Paediatric Medical Consultant should be informed asap and consider anaesthetic support early

Acute sickle chest syndrome can have a gradual onset over hours or present as an acute decompensation. It is often precipitated by a chest infection.

Acute sickle chest syndrome is likely to be multifactorial in origin with infection, thrombosis of pulmonary arteries, and fat embolism all potentially resulting in similar clinical patterns.

Regular observations, careful opiate administration, pulse oximetry and arterial blood gas sampling when oxygen saturations below 90% are recorded in air, are important in recognition of this complication.

Symptoms

- May develop during a painful vaso-occlusive limb, rib or abdominal crisis.
- Pain (often pleuritic) in chest wall, upper abdomen and/or thoracic spine.
- Dyspnoea
- Cough may be a late symptom.
- Sputum may appear bright yellow

Signs

- High fever, tachypnoea, tachycardia.
- Signs of lung consolidation, usually bilateral, generally starting at the bases.
- Bronchial breathing may be very striking. Physical signs often precede x- ray changes.

Differential diagnosis

Sickle lung and pneumonia are clinically and radiologically indistinguishable. However, consolidation in the upper and/or middle lobes, without basal changes, is suggestive of chest infection rather than sickle chest syndrome. Bilateral disease is most likely due to sickling, but atypical pneumonia should be considered. Pleuritic pain may also be due to spinal/rib/sternal infarction, or from sub-diaphragmatic inflammation.

Investigations

- Chest X-ray
- Blood culture, sputum culture, nasopharyngeal aspirate
- Consider respiratory infection serology (mycoplasma, legionella, viral)

- Arterial blood gases (ABG) if SaO2 < 90%
- Urgent Group and save, with view to early X-match if exchange transfusion felt to be likely

Management

If there is any concern that a patient is having a sickle chest crisis this MUST be discussed with the Paediatric Haematology/Oncology consultant on call at CUH promptly and the duty Paediatric Medical Consultant at NNUHFT should be informed to urgently review child. Transfer of child to CUH must be discussed early and whilst awaiting transfer, the child should be managed on HDU, if not already.

Oxygenation. Options include face mask oxygen, CPAP, ventilation

- *Top up/Plan for exchange transfusion-please discuss with CUH colleagues.*

Send emergency cross match sample and request 'sickle cell negative blood for exchange transfusion' from Blood Bank.

It may take several hours to obtain appropriate blood (blood may need to come from the National Blood Transfusion Laboratory. Therefore send this request early, if exchange is a possibility.

CPAP can be used for early disease but a worsening CXR, rapid fall in O2 saturations or persistent fever may all be indications for exchange transfusion. There should be a lower threshold for exchange transfusion if the patient has had previous chest crises or has chronic sickle lung disease.

- IV fluids as for painful sickle crisis.
- Ceftriaxone IV

From	To	Dose
1 month	11 years (up to 50kg)	50-80 mg/kg (max 4g) OD
9 years	11 years (over 50kg)	1-2g OD
12 years	17 years	1-2g OD

- Consider atypical cover with azithromycin (azithromycin is non formulary, hence requires DTMM application submission and approval; consider other macrolides if necessary).
- Review by physiotherapist (and initiate Incentive spirometry)
- Monitor oximetry on air & blood gases as indicated, pulse & respiratory rate
- Diuretics are contraindicated even though CXR and/or signs may mimic pulmonary oedema.

Definite chest crisis is likely to require a transfusion – either as top up or full exchange and must be discussed with Paediatric Haematology Consultant (see section on exchange transfusions (section 14.2)

3.4.2. Sequestration Syndromes (contact CUH team urgently)

Splenic sequestration

Splenic sequestration has a high mortality rate with some children not surviving before arriving in hospital.

Splenic sequestration is more common in infants and young children (<3 years old) and may be recurrent.

Symptoms

- May present with sudden collapse
- Abdominal pain (pulling legs up to abdomen)
- Abdominal distension

Signs

- Rapidly enlarging spleen (may or may not be painful)
- Pallor, shock (tachycardia, hypotension, tachypnoea)
- +/- Fever due to associated sepsis

Investigations

- FBC – haemoglobin generally drops by at least 2g/dl
- Reticulocyte count (raised in sequestration, absent in aplastic crisis)
- Urgent Cross match (group and Rh D compatible) anticipating may need half the patient's estimated blood volume immediately
- Blood cultures & other infection screen, as clinically indicated
- Parvovirus B19 serology (differential diagnosis is aplastic crisis)

Management

Immediate

- Resuscitation with fluids.
- Emergency top-up transfusion, with an aim to raise Hb to 8-10g/dl
- Broad spectrum antibiotics to cover pneumococcus and haemophilus: IV Ceftriaxone

Definitive

- Before discharge, teach parents to recognise the symptoms and to detect an increase in spleen size
- Consider a hypertransfusion regime for 2-3 months
- Consider splenectomy if recurrent (> 1 episode)

Hepatic sequestration

Symptoms

- Right hypochondrial pain, abdominal distension
- +/- Fever due to associated sepsis

Signs

- Enlarging tender liver, increasing jaundice
- Abdominal distension
- Collapse/shock is less common than with splenic sequestration

Investigations

- Bilirubin may be very high
- Exclude gallstones/cholestasis by ultrasound
- Blood cultures & other infection screen, as clinically indicated

Management

- May need urgent top-up transfusion
- Most cases are associated with infection – therefore empirically treat with iv co-amoxiclav
- If the patient becomes tachypnoeic, or develops chest signs, treat for sickle chest syndrome (see section 3.4.1)

3.4.3. Abdominal crisis and girdle / mesenteric syndrome

Abdominal pain is a common symptom in children.

There are a variety of clinical conditions that can result in abdominal pain.

- **Constipation** is a very common cause of abdominal pain in these patients, especially if codeine or other opiates have been used as analgesia.
- **Abdominal crisis**, characterised by abdominal distension, generalised abdominal tenderness but no rebound tenderness and diminished bowel sounds. The abdomen is not rigid and moves on respiration. Vomiting and diarrhoea are usually not prominent features.
- **Girdle (or mesenteric) syndrome** is characterised by an established ileus, with vomiting, a silent distended abdomen and distended bowel loops and fluid levels on abdominal x-ray.

Bilateral basal lung consolidation may herald the onset of an Acute Chest Syndrome.

Consider other possible surgical pathology such as acute appendicitis, cholecystitis, acute pancreatitis, biliary colic, peptic ulcer etc.

Symptoms

Abdominal crises often start insidiously with non-specific abdominal pain, anorexia and abdominal distension. Vomiting and diarrhoea are less common.

Signs

In an abdominal crisis, signs include:

- Diminished bowel sounds
- Generalised abdominal tenderness
- Rebound tenderness is absent
- The abdomen is not rigid and moves on respiration

Differential diagnoses include:

- Surgical; consider the possibility of surgical pathology such as:
  - Acute appendicitis, pancreatitis, splenic abscess, ischaemic colitis, peptic ulcer etc. Well-localised or rebound tenderness, board-like rigidity or lack of movement on respiration are suggestive of these diagnoses. In this case, ultrasound may be helpful.
  - If surgical intervention is contemplated, exchange transfusion may need to be considered prior to laparotomy, but only after discussion between the haematology consultants and the surgeons.
- Cholecystitis or biliary colic
- Splenic or Hepatic sequestration
- Urinary tract infection – more common in children with SCD
- Constipation may often co-exist, especially if codeine or other opiates have been used as analgesia
- Girdle or mesenteric syndrome (see below)

Investigations

- Chest x-ray (may need to be repeated every 1-2 days)
- Oxygen saturation
- Abdominal ultrasound as indicated
- Serum amylase to exclude pancreatitis.
- Urine M,C&S

Management

- Review by Paediatric Surgeons in all cases

Additional to analgesia and fluids:

- If there is vomiting, or if the abdomen is distended, or bowel sounds are absent, give nothing by mouth and consider nasogastric tube on free drainage and obtain surgical review
- Monitor liver and spleen size.
- If bowel sounds are absent, examine chest; abdominal X-ray and blood gases.
- If worsening jaundice, abdominal ultrasound to evaluate the biliary system
- Antibiotics: Cefuroxime, Metronidazole

If chest or girdle syndromes develop, see below.

Chest pain and pain in the spine, sternum, ribs, and/or scapula may precede full-blown sickle chest syndrome.

3.4.4. Stroke and other CNS manifestations (contact CUH urgently)

3.4.5. Stroke

- May present with fits, hemiplegia, or severe headache
- May occur at all ages, but most common in children (modal age = 7 years)
- Precipitating factors: dehydration, fever
- Sometimes in otherwise well patients

Stroke is a potentially devastating complication of sickle cell disease, most commonly occurring in individuals with homozygous disease (HbSS). Vaso-occlusion of the cerebral vessels leads to infarction, generally in the territory of the middle cerebral artery, and if untreated the majority will have a recurrence

Predictive factors for stroke include those with a history of transient ischaemic attacks, chest syndrome, hypertension, those with a low Hb F and/or a low total haemoglobin and trans-cranial Doppler (TCD) velocities of >200cm/sec.

Immediate Management

- Rehydrate immediately and give analgesia as required
- Urgent neurological assessment, and regular monitoring of neurological status
- Exchange transfusion urgently, this should be arranged whilst waiting for imaging. Aiming to achieve HbS % < 20% within 2-3 exchanges (See exchange transfusion section)
- Seizures may occur and require anticonvulsant therapy

Investigations

- MRI/CT scan of brain may be useful, if positive; but a negative scan at an early stage does not exclude brain infarction.

- Before starting exchange transfusion obtain blood for: FBC, HbS%, ferritin concentration, LFT's, and extended red cell phenotype (if not already done).
- Lumbar puncture may be necessary to exclude infection or subarachnoid haemorrhage, but must be discussed with Paediatric Haematology team first.

Follow up investigations after the acute event has resolved

- Sleep study may be appropriate
- MR angiography. The risk of recurrent neurological events is greatest in those with abnormal cerebral vasculature.
- Referrals should be made to Paediatric Neurology team, Physiotherapists, Psychologists and occupational therapy.

Follow up

Patients who have had a stroke will require a red cell transfusion programme to prevent secondary stroke, either exchange or top up (see section 14), to maintain Hb S level <30%.

They should also commence hydroxycarbamide if not already taking (see section 16.2)

3.4.6. Subarachnoid Haemorrhage

Uncommon in children, incidence rises in adolescence with median age of onset at 22years. Often associated with multiple aneurysms.

Investigation

- CT scan without contrast.
- Consider MR angiography later.

Management

- Exchange transfusion as for stroke.
- Refer to neurosurgeons.

3.4.7. Fits

Febrile convulsions may occur with high fevers, including after vaccination, however it is important to distinguish these from convulsions due to cerebral sickling. Convulsions are not uncommon following stroke or subarachnoid haemorrhage.

Investigations

- EEG
- CT or MRI
- Consider MR angiography
- Blood cultures & other infection screen, as clinically indicated

Management

Immediate:

- Treat as for stroke until proven otherwise (discuss all fitting sickle children immediately with on call consultant)
- Anticonvulsants as indicated

Definitive:

- If no abnormality on EEG, or no recurrence, no long-term intervention is necessary.
- If EEG abnormal, but CT/MRI and MRI angiogram normal; consider long term anticonvulsants on advice of Paediatric neurologists
- If infarction on scanning, or vessel stenosis/occlusion on angiogram, exchange transfuse and commence on transfusion programme.
- Refer to Paediatric neurology

3.4.8. Priapism

Priapism is defined as a prolonged unwanted painful erection with/without sexual stimulation. It is common and under reported. It is a type of compartment syndrome and if persists it is a urological emergency.

Types of presentation

Acute, fulminant (> 4 hours).

- Last several hours
- Painful
- Most have a history of stuttering priapism
- Penile ischaemia occurs after 4 hours
- Can lead to impotence – urgent urological intervention indicated.

Stuttering

- More frequent
- Less severe
- Lasts <3 hours
- Resolves on its own
- Risk of subsequent fulminant attack

Assessment

- Duration of onset
- Whether can pass urine

- Is there a history of stuttering priapism

3.4.8.1. Management of acute / fulminant priapism

This is an emergency – inform on call consultant immediately for advice.

- Rehydrate immediately – iv fluids
- Put nil by mouth (may require surgery)
- Opiate analgesia +/- sedation
- Attempt to urinate, but may need catheterisation to empty the bladder
- Urgent review by Paediatric Urology Surgeon (who will decide if to involve adult urology)
- Exchange transfusion – start organising this without awaiting surgical review.
- Discuss with UCLH urology registrar
- Pathway in appendix 5

Stuttering

- IV fluids
- Frequent emptying of bladder
- Analgesia
- Sedation, e.g., diazepam
- If no improvement by 4-6 hours, management as above.

Follow up of stuttering priapism in clinic

- Drug treatments with α-agonists (etilefrine) 25mg nocte (0.5mg/kg) can be used in the short to medium term as a preventative measure. Must be discussed with paediatric haematology consultant and pharmacy.
- (etilefrine requires individual named patient application submission to DTMM and approval-could take up to a few days to procure)

3.4.9. Aplastic crisis

A temporary red cell aplasia caused by Parvovirus B19 can lead to a sudden severe worsening of the patient's anaemia. A viral prodromal illness may have occurred, but classical erythema infectiosum ('slapped cheek syndrome') is uncommon. Aplastic crisis may affect multiple members of a family concurrently or consecutively.

The main differential diagnosis is splenic sequestration.

Diagnosis

- Rapidly falling Hb
- Reticulocytopenia (but retics may be increased if in early recovery phase)

Management

- Urgent red cell transfusion may be necessary if compromised by anaemia (if Hb < 4-5g/dl depending on steady state Hb) transfusing up to Hb 8- 10g/dl.
- Spontaneous recovery is heralded by return of nucleated RBCs and reticulocytes to peripheral blood
- Reassure: recurrence does not occur, as immunity to Parvovirus is lifelong
- Check other siblings with SCD (FBC,retics +/- Parvovirus serology)

3.5. Renal Complications

3.5.1. Haematuria

Microscopic haematuria is common in sickle cell disease. Macroscopic haematuria may be due to urinary infection, papillary necrosis and rarely stones. The passing of renal papillae may cause renal colic and ureteric blockage.

Haematuria can also occur in patients with sickle cell trait.

Investigations

- MSU for MC&S
- Ultrasound scan is the first line investigation but after discussion with radiology Intravenous urography may be necessary to establish the diagnosis

3.5.2. Urinary tract infections

These are common in particularly in girls with SCD. It should be thoroughly investigated as per any child with a proven UTI and treated to prevent serious renal pathology.

Haematuria, secondary to papillary necrosis, can precipitate UTI but other factors need to be excluded

3.5.3. Nocturia and enuresis

Nocturia and enuresis are common in part due to obligatory high fluid intake, coupled with reduced urinary concentrating capacity.

Investigations

- Reassurance, patience, and simple measures such as good bedtime routines and reward systems may be helpful. Ensure consultant in sickle cell clinic aware.
- Referral to local enuresis clinic to consider enuresis alarms and medications.

3.5.4. Hyperuricaemia

Some 15% of children and 40 % of adults have hyperuricaemia, due to a combination of decreased urinary clearance and increased production. Uric acid stones are common, as is clinical gout.

Investigations

Monitor serum uric acid

3.6. Eye complications

The ocular complications due to sickle cell disease are uncommon in children, however retinal vessel occlusion may begin in adolescence in particular in children with HbSC disease. Surveillance should begin in adolescence and by the age of 14.

For all acute visual disturbances refer urgently to the ophthalmology or eye casualty. Surgical treatment should not be undertaken without prior exchange transfusion.

3.6.1. Proliferative Sickle Retinopathy

Sickle retinopathy causes changes in the retina due to vascular damage caused by SCD, which are grouped into non-proliferative and proliferative. Infarction of the peripheral retina results in the proliferation of fragile, thin-walled blood vessels 'sea fans' at high risk of bleeding, neovascularisation. The normal age of onset is adolescence and after.

Proliferative Sickle Retinopathy: Staging criteria

Stage 1:	Peripheral arteriolar occlusions
Stage 2:	Peripheral arteriolar-venular anatomises
Stage 3:	Neurovascular and fibrous proliferations
Stage 4:	Vitreous haemorrhage
Stage 5:	Retinal detachment

Vitreous Haemorrhage and Retinal Detachment

This is more common in SC and Sβ Thalassaemia, (especially in pregnancy). Surgical treatment should not be undertaken without prior exchange transfusion.

For those patients with retinopathy or those on regular desferrioxamine, annual ophthalmology review is recommended.

3.7. Gallstones and the Biliary tract complications

3.7.1. Gallstones

Gallstones due to chronic haemolysis are common in sickle cell disease, occurring in at least 30% of children. They can precipitate painful abdominal crises and the girdle syndrome (see above).

They are often asymptomatic but can cause:

- Acute cholecystitis
- Chronic cholecystitis
- Biliary colic
- Obstruction of the common bile duct
- Related acute pancreatitis

Investigations

- Plain abdominal X-ray (as many as 50% of stones may be radio-opaque)
- Abdominal ultrasound

Differential diagnosis of RUQ abdominal pain

- Biliary colic; Cholecystitis;
- Hepatitis (viral);
- Peptic ulcer;
- Vaso-occlusive episodes;
- Hepatic sequestration;
- Chest syndrome

Management

Acute episode of cholecystitis

- Analgesia, antispasmodics
- Hydration
- Antibiotics (discuss with surgical team)

Recurrent episodes of cholecystitis is an indication for cholecystectomy

Common bile duct obstruction

Refer to Paediatric Gastroenterology / King's College liver team.

Recurrent problems (more than two attacks):

Refer for surgical opinion re elective cholecystectomy; generally laparoscopic, top up red cell transfusions to Hb 100g/L or red cell exchange transfusions may be required prior to surgery.

3.7.2. Intrahepatic cholestasis

Patients can experience episodes of severe hyperbilirubinaemia (conjugated and unconjugated) with a raised alkaline phosphatise, associated with fever and hepatic pain in the absence of demonstrable stones.

These episodes are thought to be due to severe intrahepatic sickling.

- Analgesia (care as most opiates are metabolised in the liver)
- Hydration
- Antibiotics; e.g. cefuroxime
- Monitor liver function tests, and as for girdle syndrome/hepatic sequestration

- Hyperhaemolysis +/- sequestration may supervene, requiring frequent transfusion
- In severe cases, exchange transfusion may be needed

3.8. Joints and Avascular Necrosis of hips and shoulders

3.8.1. Joint pain

Painful joints acutely are usually due to ischemia/infarction. X-rays are usually not necessary.

Differential diagnosis

- Osteomyelitis
- Septic arthritis

Distinguished by swinging pyrexia, severe systemic disorder, positive blood cultures

If there are concerns that the joint pain is not due to ischaemia then:

- Please do not aspirate joint
- If child is febrile, start antibiotics – Ceftriaxone IV 1

From	To	Dose
1 month	11 years (up to 50kg)	50-80 mg/kg (max 4g) OD
9 years	11 years (over 50kg)	1-2g OD
12 years	17 years	1-2g OD

- If child is febrile with swinging temperatures and fails to respond to antibiotics after 48 -72hr:
    1. Repeat blood cultures, ESR, CRP,
    2. Consider CT or MRI; X-ray changes of osteomyelitis may take 10-14 days to become apparent.

If osteomyelitis is felt not to be the diagnosis review antibiotics and change to oral as soon as possible or discontinue/change over according to sensitivities where appropriate.

Note: swellings over long bones, muscles, and joint effusions are common in vaso-occlusion. **Do not aspirate joints as a first line investigation.**

However in the chronic situation if pain is repeated, or prolonged, X-ray 8 – 12 weeks after the episode to exclude aseptic necrosis

3.8.2. Avascular necrosis of hips and shoulders

Occurs in approximately 15% of all patients. The normal age of onset is adolescence and it is more common in SC and Sβo.

Presentation

- Pain in the hip, leg, groin, or knee on movement; later at rest. Repeated or prolonged pain (> 8 weeks) should be investigated for aseptic necrosis.
- Limitation of movement; particularly abduction and external rotation of the hip, external rotation of the shoulder.

Investigations

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

Management

- Analgesia with non-steroidal anti-inflammatory agents
- Rest and the avoidance of weight bearing
- The role of transfusions remains uncertain. Transfusion cannot reverse the process but may prevent progression to the contralateral joint; it is performed pre-operatively and for 3 months post-operatively to maximise bone healing.
- Refer for orthopaedic assessment and treatment, which is likely to involve these types of treatment:

Osteotomy and/or decompression surgery may be considered. Major joint surgery may be necessary if pain is continuous (>2 years) or very severe, or if the patient's mobility is seriously affected.

Different types of prosthesis, hip fusion, or bone grafting are used depending on the individual case. Cemented prostheses are best avoided. Loosening of the prosthesis is quite common. Infection is not uncommon.

The possibility of failure, the likelihood of some residual pain, the potential life of the prosthesis, and the limitations imposed must always be discussed with the patient pre-operatively.

3.9. Transfusions

3.9.1. Simple top up

This is required when the haemoglobin falls to less than 45 g/dl due to sequestration, an aplastic crisis or haemolysis. It may be indicated for acute chest crisis, but only after discussion with the on call paediatric haematology consultant.

Aim: To raise Hb by 3 g/dl per transfusion.

3.9.2. Exchange transfusion

Exchange transfusion is undertaken to rapidly reduce the percentage of sickle cells in the circulation when a patient develops a life-threatening complication of sickle cell disease. It should only be undertaken under instruction from on call consultant, as

the possible complications are considerable. However, patients with the following problems justify the risks:

- Severe chest syndrome (e.g. low or falling PaO2) or Girdle syndrome
- A new CVA (or suspected)
- Multi-organ failure, e.g. associated with systemic fat embolism
- Fulminant priapism unresponsive to pharmacological therapy (as impotence can be the long-term outcome)

Exchange transfusions should only be undertaken by experienced medical and nursing staff and in the unwell patient it should be performed on HDU or PICU-within the Eastern region, this procedure is ONLY performed at CUH for children.

Elective exchange transfusions can be undertaken in the children's inpatient wards or in the paediatric day unit by experienced medical and nursing staff- this is ONLY done at CUH for children.

Aim:

1. To reduce the % of Hb S to < 20% - over 2-3 exchanges unless acutely ill, when more rapid exchange may be appropriate
2. To keep Hb < 10g/dl initially (or at steady state level in those with higher baseline Hb, e.g. HbSC patients), **~125g/l and PCV 0.36** by the end of the whole procedure.

   (Note: The haematocrit of the donor blood is approximately double that of the patient.)
3. To maintain a steady blood volume in the patient throughout the procedure.
   - SAG-M blood, which is the freshest available (to prolong its life in the patient).
   - The red cells used should be specially grouped (ABO compatible, Rh negative (rr) or RO as appropriate, Kell compatible), and HbS negative.
   - Do not use diuretics.
   - Continue to administer IV fluids at the standard rate between transfusions.

Preliminary investigations

- FBC
- % HbS, but do not wait for result before starting exchange.
- Extended RBC phenotype (if not already known),
- Xmatch 4 – 6 units blood
- U & Es, Ca++
- Arterial blood gases – in those with symptoms suggestive of chest or girdle

syndrome,

- Serology for Hepatitis B & C, if not done recently.

All patients requiring an exchange transfusion must be discussed with the Paediatric Haematologist/Oncologist on call. Exchange transfusions for <16 years of age are done at CUH only.

The methods of exchanging can be either automated or manually. An automated exchange is the preferred option but may only be possible during working hours.

3.9.3. Automated exchange

This will be organised by Consultant Paediatric Haematologist. The patient will require central access.

3.9.4. Manual exchange

Requires Venous / central access

Volumes required
The initial aim is to exchange 1.5 - 2 times the child's blood volume, divided over 2-3 procedures. **Volume (ml) of SAG-M blood for each exchange** should be:

30 x weight (in kg) = volume in mls,
(30 ml/kg is the approximate red cell mass from infancy to teenage years).

The volume of blood venesected should be replaced with a combination of saline and blood. Packed red cells have double the haematocrit of normal blood, and so there is a risk of raising the Hb/Haematocrit of the patient to dangerously high levels if this is not taken into account.

The Hb should therefore be checked at the end of the exchange to ensure the Hb is not over 125g/l.

Two ports of venous access are required; one for venesection, the other for administering blood and crystalloid.

In emergency it is advisable to use a central line, or arterial line (on PICU), for venesection.

- The aim is that this should be an isovolaemic (equal volumes in and out) procedure with frequent, monitoring of blood pressure, heart rate and oxygen saturations every 15 minutes, and 1 hourly temperature monitoring
- If the Hb is less than 60g/l, start by giving a simple top up to 80g/l. Then continue with venesecting one third of the volume in mls of the total to be exchanged, replacing with normal saline simultaneously, at the same rate. Each one third ‘aliquot’ should be exchanged over 30 – 45 mins.
- Then continue exchange: venesecting and replacing each aliquot with blood, at the same rate.

- Aim to complete each exchange over 2 – 3 hours.

Ensure Hb does not rise above 125g/l.

Check FBC, HbS %, urea and electrolytes including calcium. If HbS not < 20%, then consider continuing with further exchanges (daily), to give a final Hb of 125g/l and Hb S ideally between 10% and 20%.

Critically ill patients may require exchanges to be at more frequent intervals. Where possible, leave a 4-8 hour break between exchanges. In the very sick patient, the procedure is a continuous process. In these patients, particular attention should be paid to the pO2, CVP, acidosis, Ca2+, citrate load, core temperature, and clotting.

3.9.5. Regular transfusions, i.e. hypertransfusion

These are for patients with severe complications of sickle cell disease, in particular:

- Stroke, & other CNS complications
- Chronic organ damage such as chronic renal failure or chronic lung disease
- Failure to thrive (when causes other than sickle cell disease have been excluded) or delayed puberty
- Intractable or very frequent painful crises

The objective is to keep the HbS less than 30%. This can be achieved by regular top-up (or additive) transfusions keeping the Hb between 100 and 120g/l, as in patients with β Thalassaemia major. Regular exchange transfusions may also be undertaken in some circumstances. There are both advantages and disadvantages to performing regular exchange transfusions, which are equally effective in reducing complications of sickling and cause less iron accumulation; however, they are associated with higher donor exposure and require excellent venous access.

Investigations to be performed 1 or 2 days prior to admission for transfusion

- FBC
- % HbS,
- Crossmatch
- U+Es, LFTs

Ensure patient has been or is being vaccinated against hepatitis B and check Hepatitis C antibody status prior to embarking on regular transfusions

For top-up transfusions **the volume of SAG-M blood required**

(ml) is: $(Hb_{desired} - Hb_{current}) \times \text{weight (kg)}$

x 0.4

Do not attempt to raise the haemoglobin by more than 4g/dl at any one transfusion.

The rate of transfusion should be 5mls/kg per hour and not more than 150mls/hr
Post-transfusion, check FBC and % HbS.

Blood Products

Give: Sickle negative, ABO compatible, Rh and Kell compatible (or K neg) cells.

Do not use diuretics

Possible immediate problems of transfusion

1. **Anaphylactoid reactions** due to anti-WBC/platelet antibodies. Treat as NHTR (non-haemolytic transfusion reaction) with antihistamines, etc.
2. **Metabolic disturbances** are rare; occurring in small children, or in association with acute visceral sequestration requiring continuous exchange. Treat as for massive transfusion.
3. **Fitting** is very rare. Usually a sign of cerebral sludging; often in patients with previous CNS problems.

   Care that PCV has not risen too fast or too high. Give anti-epileptics, ensure there is a large fluid intake and oxygen, and check that the PCV is < 40%.
4. **Hypertension** is occasionally seen in patients with circulatory overload, particularly when the blood is transfused through a central line. Monitor the BP closely.

   If there is a rise in the diastolic pressure > 20 mm Hg:

   a. Slow down the exchange rate
   b. Check that the PCV is < 40%.

   If the diastolic BP continues to rise, or is > 100 mg Hg, stop the exchange, give anti-hypertensive treatment, venesect, give prophylactic (fast acting) anti- epileptics.

3.10. Surgery and Anaesthesia considerations (in the Eastern region, this is ONLY done at CUH for children)

Surgery should be undertaken with close liaison between the surgeon, anaesthetist and paediatric haematology staff.

Procedure for surgery

- Admit and warn the patient that they may need to remain in hospital for at least one night postoperatively.
- Start IV fluids when oral fluids are stopped and continue until patient is able to take fluids freely.
- Ensure careful oxygenation from pre-medication, throughout the operation,

and at least until fully awake. (Monitor using SaO2 from the recovery room until 24 hours post operatively)

- Hyperoxygenation (use of 100% O2) at induction and reversal of anaesthesia.
- Ensure appropriate analgesia
- Keep the patient warm at all times.

For patients with HbSS and HbS/β0 thalassaemia undergoing low- and moderate-risk surgery, a preoperative top-up transfusion to a target Hb of 100 g/L significantly reduces perioperative complications, particularly acute chest syndrome and is as effective in preventing perioperative complications as an aggressive exchange regimen that reduced HbS to <30%.

The perioperative management of children with HbSC disease, or with a baseline Hb >90 g/L, is less clear, particularly in low- or moderate-risk surgery, and needs to be decided on an individual basis.

3.11. Exchange transfusion

Exchange transfusion is not usually required unless the patient has a serious chronic complication (e.g. chronic renal failure, liver disease, or chronic sickle lung).

Major surgery (including cardiovascular surgery and neurosurgery) typically requires transfusion, usually with an exchange transfusion to reduce the HbS level <30%.

Exchange transfusion will be organised by the Consultant Paediatric Haematologist close to the date of surgery, which should not thereafter be cancelled!

3.12. Outpatient management

The aims of outpatient management are:

- To monitor the medical, educational and psychological progress of the child
- Early recognition of complications and update on intervention as required
- To establish baseline observations for comparison in acute illness.
- To provide education and support to the child and their family.
- To discuss genetic referral if appropriate/required

The majority of new patients will have been identified by the newborn screening programme or will have been referred when moving into the region. Results of newborn screening when an infant may have a type of sickle cell disorder are sent to the local paediatrician and to the specialist centre.

The generic email for results being reported is: **add-tr.cuhpaedhaem.nmh@nhs.net**

This will be monitored by the NMH CNS team. The NMH CNS team will support the updating the NHR. When the patient has had their diagnosis the CNS will send a

letter to the parent with contact details and some information about attending for clinical appointments.

Handbook for Sickle Cell and Thalassaemia Screening is the guideline detailing newborn screening, interpreting results, confirmatory testing and the time frames and standards.

All new patients should see their local team to discuss diagnosis and to start antibiotic prophylaxis. They will be invited for specialist clinical review and support appointment before they are 3 months old or within 3 months of referral.

At the initial appointment confirm that the patient is taking prophylactic antibiotics and have been offered folic acid.

Penicillin V	Age
62.5mg BD	<1 year of age
125mg BD	1-4 years of age
250mg BD	≥5 years of age

Folic Acid	Age
500 micrograms/kg (max 5mg) daily	0-11months of age
5mg daily	≥1 year of age

Explain the natural history of the disease at each stage: infancy, early childhood, adolescence and puberty and discuss specific complications such as:

- Dactylitis
- Splenic sequestration
- Painful Crisis
- Acute chest syndrome
- Stroke

Demonstrate how to palpate a spleen in order to identify splenic sequestration.

Discuss strategies for keeping the child well such as completing the childhood vaccination programme, including the additional pneumoccal and Meningitis ACWY vaccines, annual flu vaccine, prophylactic antibiotics, avoidance of exposure to the cold, keeping well hydrated, having appropriate analgesia when needed and the importance of clinical review when unwell or pyrexial and participation in ongoing surveillance.

Ensure the family have contact numbers for the GP, Health visitor, local hospital team and the specialist teams.

Discuss the purpose of the National Haemoglobinopathies Registry and the sharing of data

If confirmatory blood samples are still required these are sent to the Haemoglobinopathy Screening laboratory:

Central Middlesex
Hospital Acton Lane
London
NW10 7NS

Tel: 0208 453 2671

LNWH-tr.CMHscreening@nhs.net

New patients should have baseline bloods to include:

- FBC
- Retics
- Hb electropheresis
- LFT
- Electrolytes
- G6PD
- Group and screen
- Extended red cell phenotyping
    - +/- vitamin D levels

Routine bloods should include: FBC, retics, LFT's, electrolytes and vitamin D levels + those as clinically indicated (e.g. Hb electrophoresis for those on hydroxycarbamide).

3.12.1. Follow-up / Annual review (Annual reviews/TCD's are done at CUH for children in this region)

All under 2's should be reviewed 3-4 monthly, under 5's 6 monthly and older children should be seen at least annually for clinical review (or more frequently if their clinical condition suggests).
The review should include taking a history, clinical assessment, assessment of growth, development, clinical observations and clinical examination.

A Transcranial Doppler scan (from the age of two until 16 years of age) should be completed yearly (and more frequently if clinically indicated). Transcranial Doppler scanning clinics are currently held 6 times per year on Saturdays.

The annual haemoglobinopathies flowsheet on epic should also be completed to enable data and audit collection.

Issues covered should include:

- Review of information provided by the LHT including any investigations undertaken and treatment given

- Clinical review:
  - number of hospital admissions
  - number and severity of painful episodes (including days off school)
  - other complications e.g. splenic sequestration, aplastic crisis, priapism, gallstones, chest syndrome, stroke
  - nocturnal enuresis in children aged >6 years
  - assessment of child development
  - (for children on regular transfusions) blood volume transfused in past year
- review of infection prevention:
  - penicillin V dosage and compliance
  - immunisation record
  - (for children on regular transfusions) hepatitis A, B and C serology, including Hep B surface antibody titre, and CMV serology
- clinical tests (undertaken at visit or performed since last review):
  - clinical examination of heart, lungs, liver and spleen
  - assessment of growth and development
  - blood pressure
  - oxygen saturation
  - urinalysis, including urine albumin:creatinine ratio
  - ferritin
  - (for children on regular transfusions) pre transfusion HbS percentage
  - TCD screening and risk of stroke (for children on regular transfusions for cerebrovascular disease)
- Confirm requirements and results of MRI/magnetic resonance angiogram (MRA) of brain (for children on regular transfusions) T2*MRI heart and ferriscan of liver
- The annual review provides an opportunity for collection of data as suggested by the NHR.
- Provide education, Patient Information Leaflets and appropriate web-links
- Referral to other healthcare professionals (e.g. dietician / physiotherapy / psychology) and support with external agencies (e.g. housing, education and welfare support)
- All children should be offered a careplan / advice which can be shared with school
- Consideration and discussion of other treatments e.g. hydroxycarbamide, stem cell transplantation.

3.12.2. Hydroxycarbamide

Hydroxycarbamide should be discussed at each visit and offered to all children from the age of 9 months of age regardless of clinical status.

Hydroxycarbamide should be commenced at a dose of 20mg/kg. Bloods for FBC, retics, electrolytes and LFTs should be monitored monthly to 3 monthly

After 8-12 weeks the dose can be escalated by 5-10mg/kg until a maximum of 35mg/kg or a maximum tolerated dose

(Hydroxycarbamide guideline BSH appendix 4)

3.12.3. Other considerations

Patients and families considering Stem cell transplant and gene therapies can be referred to the team at St Mary's Hospital (tissue type the patient and siblings before this)

Preparation for transition to adult haematology services should begin at aged 14 and transfer of care will be to the specialist Adult Haemoglobinopathy team after the age of 16.

Travel Requirements

Advice from CAA website regarding flying with haematological disorders:

"Patients with a haemoglobin of greater than 8 g/dl may travel without problems assuming there is no coexisting condition such as cardiovascular or respiratory disease. If the haemoglobin is less than 7.5 g/dl, special assessment should be made and the use of supplemental oxygen should be considered.

"Individuals with chronic renal insufficiency or other medical condition predisposing to anaemia, which is chronic in nature, will usually tolerate a lower haemoglobin level than if the anaemia is of acute onset. Sickle cell trait does not present a particular problem at normal cruising altitude. However, patients with sickle cell anaemia should travel with supplemental oxygen and should defer travel for approximately 10 days following a sickling crisis."

Children with Sickle cell disease should receive:

- Meningitis ACWY if travelling to sub-Saharan Africa and Saudi Arabia if not already received
- Other recommended travel vaccinations for the country being visited
- Malaria prophylaxis

4. Related Documents

- Children's pain management – NURSE controlled analgesia (NCA) procedure
- Children's pain management – PATIENT controlled analgesia (PCA) procedure

5. References

- Cope A, Derbyshire P. Sickle cell disease, update on management Paediatrics and Child Health 2013; 23:11; 480-485
- NICE Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. NICE clinical guideline 143 2012
- RCGP Summary of antimicrobial prescribing guidance – managing common infections January 2024
- PHE (2018) Newborn screening. (Guidance)
- PHE (2019) Sickle Cell Disease in Childhood: Standards and Recommendations for clinical care. 3rd ed.
- Qureshi A, Kaya B, Pancham S, et al. Guidelines for the use of hydroxycarbamide in children and adults with sickle cell disease: A British Society for Haematology Guideline. Br J Haematol 2018; 181: 460–75.
- Trompeter S, Massey E, Robinson S (2020) Guideline 'Red blood cell specifications for patients with hemoglobinopathies: a systematic review. A British Society of Haemtology Guideline. Br J Haematology 2020; 189, issue 3: 424-427.
- Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle-cell anaemia: a multicentre, randomised, controlled trial (BABY HUG). Lancet 2011; 377: 1663–72.
- Ware RE, Davis BR, Schultz WH, et al. Hydroxycarbamide versus chronic transfusion for maintenance of transcranial doppler flow velocities in children with sickle cell anaemia—TCD With Transfusions Changing to Hydroxyurea (TWiTCH): a multicentre, open-label, phase 3, non-inferiority trial. Lancet 2016; 387: 661–70.
- Ware RE, Helms RW. Stroke with transfusions changing to hydroxyurea (SWiTCH). Blood 2012; 119: 3925–32.
- Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014; 312: 1033–4.

6. Monitoring Compliance

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
Audit of compliance of inpatient management with the standards set out in this document, and by review of incident	Monitoring will take the form of regular audit of compliance of inpatient management with the standards set out in	Audit of compliance of inpatient management	clinical governance departmental meetings	3 yearly or earlier in the light of new evidence

reports in the Trust pertaining to children with sickle cell disease	this document, and by review of incident reports in the Trust			

An audit against standards within guideline will be conducted in line with the Trust's audit department and presented to the Paediatric Medicine departmental Governance meetings who will ensure that the actions and recommendations are suitable and sufficient.

7. Appendices

7.1. Appendix 1: Prescribing guidelines in Paediatric Sickle Cell Pain

Assess child immediately **If patient under 1 year, doses will need to be reduced** **Use liquid preparations for rapid absorption**
MILD PAIN (score 0 to 3) • Maintenance oral hydration • **Paracetamol** 20mg/kg STAT, **then** 15mg/kg 4-6 hourly max. qds, regularly • **reassess after 30 min / 1 hour** • if pain controlled – dischargee on usual analgesia and inform haematology team if pain NOT controlled treat as moderate – (pain score of 4 to 7)
MODERATE PAIN (score 4 to 7) • maintain oral hydration • treat as **mild** pain **and add** • **Ibuprofen** 7.5mg-10mg /kg 8hrly (max 400mg TDS) – unless contraindicated • If pain controlled – discharge on analgesia and inform haematology team • **If pain not controlled add Oramorph (morphine sulphate oral solution)**, STAT dose 300mcg/kg **(up to max dose of 20mg)** • Reassess after 30 minutes • if pain NOT controlled treat as **severe** (pain score of 8 to 10) – child will need admission
SEVERE PAIN (score 8 to 10) • oral/intravenous hydration • if pain controlled – admit, treat with paracetamol, ibuprofen and PRN Oramorph 300mcg / kg, 3 hourly (max 20mg per dose) • If pain NOT controlled, admit and give immediate top up dose of Oramorph (100mcg/kg) and call pain team to initiate PCA/NCA **Contact Consultant**
Reassess after 30 minutes
Pain still not settling • Intravenous hydration • to commence PCA continuous infusion • NCA Infusion if under 6 years old • Monitor for respiratory depression

7.2. Appendix 2: Flowsheet of management of acute presentation in children with Sickle Cell Disease

7.3. Appendix 3: Immunisations

Children with SCD should follow the UK schedule of routine immunisations, which is updated regularly in the 'Green Book'. Children arriving in the UK after the newborn period who have not received the complete vaccination schedule should follow the guidance provided in the document Vaccination of individuals with uncertain or incomplete immunisation status.

Children with SCD are also recommended to receive the following additional vaccinations:

- For a child diagnosed in the first year of life, two doses of menacwy 1 month apart (in practice this probably means giving two doses of menacwy in the second year of life)
- For children not given Prevenar 13 (a pneumococcal conjugate vaccine, also sometimes called PCV) during the first year of life, two doses of Prevenar 2 months apart in the second year
- For all children aged 6 months to 2 years, the intramuscular flu vaccine
- For all children aged 2 years to 17 years (the licensed age groups), Fluenz tetra nasal spray (a live attenuated vaccine), given annually – increasing numbers of children will receive this vaccination in school as the programme is gradually rolled out to children without specific conditions
- Polysaccharide pneumococcal vaccine (PPV) at 2 years and 5 yearly thereafter.

Although all children are now offered the conjugate pneumococcal vaccine Prevenar 13, there is evidence of a rise of infections causing invasive pneumococcal disease that are not prevented by vaccination and emphasis must remain on children continuing to take regular penicillin in addition to immunisations1.

Furthermore, in order to ensure maximum coverage with PPV, there needs to be a robust local system for policing the administration and recording of the PPV vaccine; consideration should be given to administering this at the hospital appointment, as is done in some large units, particularly in London, rather than in primary care.

7.4. Appendix 4: Hydroxycarbamide Dosing

Hydroxycarbamide dosing protocol from BSH guideline, May 2018 Baseline FBC, retics, HbF % and renal function

Pregnancy test in post pubertal females

Start at 20mg/kg (tablets are 500mg, liquid is 500mg/5ml) Repeat FBC at 2w for toxicity

Bloods after 8-12w and increase dose if following parameters are met: N >2 / Plt >150 / Hb >60 / Retics >80

Increase in 5mg/kg/d increments every 8-12w up to 35 mg/kg

Repeat FBC at 2 weeks after each dose increase, once dose stable monitor FBC, retics, HbF %, renal function and LFTs every 8-12w

Interrupt therapy if N <1.0 / Plt <80 / Hb <45 / Retics <80 with Hb <90 Repeat FBC weekly until N >1 / Plt >80 / Hb >45 / Retics >80 with Hb <90

Consider restarting at same dose if transient cytopenia, or restart at a dose 5mg/kg/d lower.

Note update from the pharmaceutical company July 2020: Dear Healthcare Professional,

RE: Xromi® (Hydroxycarbamide) 100 mg/ml oral solution

Xromi® (Hydroxycarbamide) 100 mg/ml oral solution has been authorised for the prevention of vaso-occlusive complications of sickle cell disease in patients over 2 years of age.

We would like to inform you that we have reissued the Physician's Guide and Patient/Parent Guide as part of the risk management materials for Xromi® (Hydroxycarbamide) 100 mg/ml oral solution to align the information included in the materials to the approved and updated Product Information:

- Toxic ranges for neutrophil counts were agreed to be lowered to 1,500 cells/ mm3 (threshold for neutropenia) and intervals for blood cells monitoring at initiation of treatment extended to one month (Section 4.2).
- The requirement to follow-up the growth of treated children and adolescents has been removed (Section 4.4).
- Parvovirus B19 infection has been removed as a side effect (Section 4.8).
- Recommendation that blood counts are monitored for several weeks after overdose since recovery may be delayed (Section 4.9).

Consequential changes were applied to the Package Leaflet:

- Section 3 was updated to extend the intervals for blood cells monitoring at initiation of treatment from two weeks to one month.
- Section 4 was updated to remove Parvovirus B19 infection as a side effect.

Please replace the previous versions 001 you received with the current versions:

- XromUK002 June 2021 (Physician Guide)
- XromUK002 June 2021 (Patient/Parent Guide)

The MHRA-approved risk management materials outline important information on minimising the risk of serious adverse events and monitoring requirements. Please keep this guide, and the Patient/Parent Guide, in a safe place for future reference.

Copies of the guides can be downloaded from: https://www.medicines.org.uk/emc/rmm-directory/

The Summary of Product Characteristics and the Patient Information Leaflet can be found here: https://www.medicines.org.uk/emc/product/10549/smpc

Further information can be obtained by emailing Nova Laboratories at: xromi@novalabs.co.uk

For more information please contact Nova Laboratories Ltd.

T: +44 (0) 116 223 0100

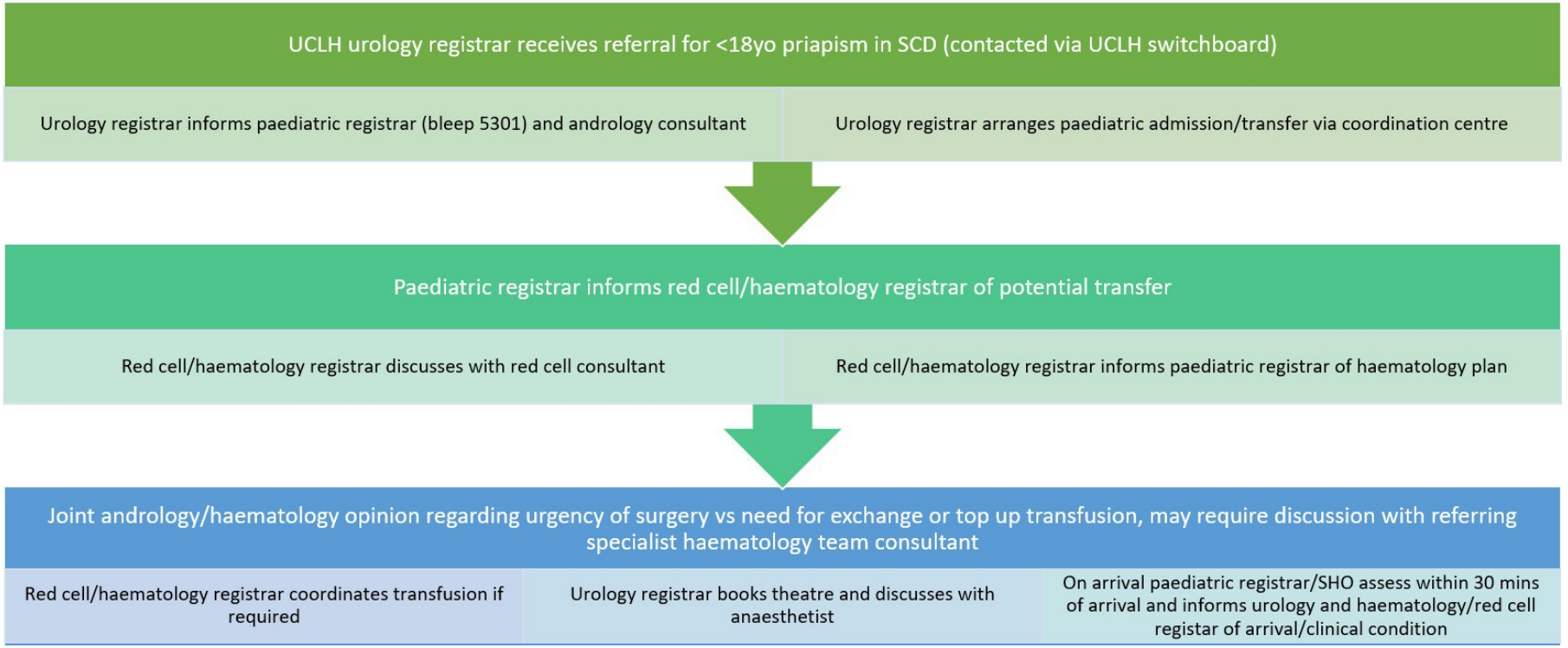
F: +44 (0) 116 223 0101

E: info@novalabs.co.uk

7.5. Appendix 5: Priapism Pathway

The Red Cell Network
Haemoglobinopathy Coordinating Centre

Paediatric Sickle Cell Priapism Pathway



8. Equality Impact Assessment (EIA)

Type of function or policy	Existing

Division	W&C	**Department**	Paediatrics
Name of person completing form	Jo Ponnampalam	**Date**	October 2024

Equality Area	**Potential Negative Impact**	**Impact Positive Impact**	**Which groups are affected**	**Full Impact Assessment Required YES/NO**
Race	no	no	none	no
Pregnancy & Maternity	no	no	none	no
Disability	no	no	none	no
Religion and beliefs	no	no	none	no
Sex	no	no	none	no
Gender reassignment	no	no	none	no
Sexual Orientation	no	no	none	no
Age	no	no	none	no
Marriage & Civil Partnership	no	no	none	no
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.