CLINICAL GUIDELINE TITLE	Paediatric Sickle Cell Disease

1) SUMMARY

This guideline covers the management of clinically significant sickle cell disorders in children and is directed at all clinical staff involved in the care of children with sickle cell disease (SCD). SCD is associated with multiple disease-related complications the effective management of which require a multidisciplnary approach. The most common indication for admission is acute painful crisis treatment which should follow NICE guidance. Most children with SCD will have been under follow-up but all new patients who present with suspected SCD should be fully assessed to confirm the diagnosis and agree an individual management plan. All children with SCD require regular follow-up to detect or prevent complications and identify the need for disease-modifying therapy. The patient and family should receive full and accurate information with support from experienced professionals.

2) INTRODUCTION

Sickle cell disease (SCD) comprises a group of conditions due to inheritance of the sickle gene and is now the most common genetic disorder in the UK with a birth prevalence of 1 in 2400. In developed countries most affected children survive to adulthood. Prompt recognition and treatment of acute complications and early detection of secondary complications underpin effective clinical management of SCD.

3) DEFINITIONS

A&E	Accident and Emergency
ACS	Acute chest syndrome
APLS	Advanced Paediatric Life Support
CMV	Cytomegalovirus
CNEP	Continuous negative extrathoracic pressure
CNS	Clinical Nurse Specialist
CNS	Central Nervous System
CPAP	Continuous positive airways pressure
CRP	C-reactive protein
CT	Computerised tomography
CVA	Cerebrovascular Accident
CVS	Cardiovascular System
DFO	Desferrioxamine
DFP	Deferiprone
DFX	Deferasirox
FBC	Full Blood Count
HIV	Human immunodeficiency virus
IV	Intravenous

LDH	Lactate dehydrogenase
LFT	Liver Function Test
MRI	Magnetic resonance imaging
MSU	Mid-stream urine
NCA	Nurse controlled analgesia
PA	Personal Assistant
PCA	Patient controlled analgesia
PHD unit	Paediatric Haematology Day Unit
PRN	As and when needed
PSSU	Paediatric Short Say Unit
SAE	Serious Adverse Effect
SCD	Sickle Cell Disease
SHO	Senior House Officer
SpR	Specialist Registrar
TCD	Transcranial Doppler
TCDi	Transcranial Doppler Imaging
U&E	Urea and electrolytes
UTI	Urinary Tract Infection

4) SCOPE

This guideline is directed at all clinical staff involved in the care of children with sickle cell disease (SCD). It applies to all patients known to have or who are diagnosed with SCD. SCD includes sickle cell anaemia (HbSS) as well as those compound heterozygous states (HbSC, HbSD, HbSO-Arab and sickle β-thalassaemia) and other less common conditions that give rise to a clinically significant sickling disorder. The guideline describes the clinical management of SCD. It should be read in conjunction with NICE Guidance on the management of sickle cell acute painful episode (http://guidance.nice.org.uk/CG143), BCSH Guideline on the management of Acute Chest Syndrome in Sickle Cell Disease 2015 (http://onlinelibrary.wiley.com/doi/10.1111/bjh.13348/epdf).

5) FULL GUIDELINE

Appendices:

PAEDIATRIC HAEMATOLOGY / SICKLE CELL TEAM

St Mary's Hospital (Switchboard: 020 3312 6666)		
Dr Kirstin Lund	Imperial College Paediatric Red Cell Disorders Network Lead	Ext: 27682 PA: Ext 26157
Vacant Position	Imperial College Paediatric Red Cell Disorders Network Deputy Lead	Ext PA: Ext
Ms Catherine Mkandawire	Paediatric Haemoglobinopathy CNS	020 3312 3346 Mobile 07795 951 153
Paediatric Haematology SpR	Rotates 6- monthly	Bleep 2262/2261
Paediatric Haematology Clinical Fellow	Rotates 6- monthly	Bleep 2262/2261
Paediatric Haematology SHO	Rotates 6- monthly	See rota
Paediatric SpR (out –of-hours)	See rota	Bleep 1202
Paediatric SHO (out-of-hours)	See rota	Bleep 1228
Other key staff		
Dr Mark Layton	Consultant Haematologist (Adult Haemoglobinopathy)	020 3313 1320
Dr Helen New	Consultant Paediatric Haematologist (Transfusion and Coagulation)	Secretary: Ext 26164
Dr Leena Karnik	Consultant Paediatric Haematologist	Secretary: Ext 26157
Dr Josu de la Fuente	Paediatric Blood and Marrow Transplant Programme Director	Ext 21999 PA: Ext 26164
Ms Lorry Phelan	Haemoglobinopathy Scientist lead for Laboratory	Ext 21130
Ms Lydia Alexander	Haemoglobinopathy CNS (Adults)	020 3313 8372
Ms Corrine Bedlow	Lead Nurse Paediatric Haematology	Ext: 23345
Becky Armstrong	Paediatric Clinical Psychologist	Ext: 26164
Ms Vesna Graham	Community Haemoglobinopathy counsellor	020 3315 2980 / 2375
Ms Zita Noone	Haemoglobinopathy social worker	020 3313 4655

Sickle Cell Society
Address: 54 Station Rd,
Harlesden, NW10 4UA
(020 8961 7795/4006)
website: www.sicklecellsociety.org
e-mail: sicklecellsoc@btinternet.com

CONDITIONS REQUIRING IMMEDIATE ADMISSION

- Agonising pain (i.e. requiring opiate analgesia)
- Increased pallor, breathlessness, exhaustion
- Marked pyrexia (> 38 ^{o}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 or any abnormal CNS signs
- Priapism (> 4 hours)

Inform specialist haematology and paediatric registrar on-call, who will discuss with the consultant.

ADMISSION PROCEDURE

Children are seen in the paediatric A&E by either the A&E SHO or A&E SpR. The relevant paediatric SHO/SpR should see the patient as soon as possible (certainly within 1 hour). During working hours the Paed Haem SpR should see the child in A&E. In the event this is not possible they should be seen within an hour of arrival on to the ward. If the patient is clearly in a painful crisis, analgesia (see page 9) should be administered **within 15 minutes** of arrival in A&E. Children may be admitted to the PSSU when inpatient admission is thought not to be required but they require monitoring for a short period of time. Analgesia may precede the taking of a more detailed history. The Paed Haem SpR (or out of hours the Paediatric On-Call Team) should be informed of all children admitted. The Paediatric Haemoglobinopathy CNS and Paed Haem SpR should also be informed of all children attending A&E and then discharged so follow up can be arranged.

1. Clinical Assessment

A full history and examination must be carried out, paying particular attention to symptoms/signs of life-threatening complications including acute chest syndrome, splenic sequestration or aplastic crisis, or septicaemia.

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

The following should be recorded in the notes:

- 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
- Liver and spleen size (cm)
- Degree of pallor, blood pressure.

Case Notes.
The case notes of children with sickle cell disease are mainly kept in Paediatric Reception on the sixth floor QEQM building, and can be obtained via the ward clerks. Children who attend regularly have their notes stored in the PHD unit. Some sets of notes may be with Paediatric Haematology PA (extension 26157) whose office is in the Bays Building.

2. Discharge from Casualty or Ward

If there are no other indications for admission, following discussion with the Haematology SpR (out of hours Paediatric SpR) or CNS, a child can be discharged from A&E, PSSU or from the PHD unit with:

- A supply of oral analgesia
- Instructions to drink 150 mL/kg/day
- A follow-up appointment for review, within a week, either on the PHD unit or the next available Paediatric Haematology Clinic (Monday pm), or by the Paediatric Haemoglobinopathy CNS if appropriate. Shared care patients may be arranged to be reviewed by their local teams where appropriate.
- Folic acid
- Prophylactic penicillin V (erythromycin bd if penicillin allergic)
- Antibiotics if there is any evidence of infection (refer to hospital antibiotic policy). If not, may suggest doubling normal penicillin prophylaxis for period when unwell.
- Discharge letters should be copied to the named consultant of local hospitals of all shared care patients. The Paediatric Haematology CNS will also inform the referring team of the patients' admission and discharge.

Social support/assessment:
Inform: The child's sickle cell counsellor/community sickle nurse should be informed on admission *and* receive a copy of the medical discharge letter. Zita Noone is also available for social work issues as required.

SICKLE CELL CRISIS: INVESTIGATIONS

1. Routine Investigations (All cases)

Blood Tests

- FBC & reticulocytes
- Group, screen and save
- Urea & electrolytes
- LFTs, LDH
- CRP
- Blood cultures (if any symptoms/signs of infection)

Microbiological screen

- Urine dipstick & MSU culture
- Viral & atypical pneumonia serology 'to store'
- Other cultures as indicated (See below)

Other tests

- Venous gas
- Pulse oximetry (SaO_2) in air
- Chest x-ray if indicated (i.e. symptoms/signs)

2. Additional Investigations

Certain tests are done if indicated, as follows:

Test	Indication
Serum amylase Abdominal ultrasound	Abdominal symptoms/signs Symptoms suggestive of cholecystitis
Screen stool for *Yersinia* (special stool cultures) and *Klebsiella (normal stool cultures)* Serum for *Yersinia* antibodies	Patients on desferrioxamine (DFO) with diarrhoea/abdominal pain (STOP DFO)
Mycoplasma and Chlamydia serology	Evidence of chest involvement
Parvovirus B19 IgM and IgG serology and PCR	Fall in Haemoglobin with low reticulocytes
CT/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
HbS level	ONLY If patient is on regular transfusions AND ACS, girdle syndrome or stroke suspected or an exchange transfusion considered.

*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. Early involvement of orthopaedic surgeons should be arranged if osteomyelitis is suspected. MRI scan is the investigation of choice in suspected bone and joint infection and should be arranged as soon as possible. X-rays can be useful in confirming avascular necrosis as a cause of chronic or intermittent pain.

3. New Patients to the Hospital Require all the Routine Investigations

Additional Blood Tests

- Hb, reticulocytes, blood film
- HPLC
- α and β globin mutation analysis
- Red cell genotype
- G6PD
- U&E, LFTs, bone profile, LDH
- Vitamin D
- Ferritin
- Hepatitis B and C serology
- Parvovirus B19 serology
- *Consider HIV serology*

PAINFUL SICKLE CELL CRISIS: MANAGEMENT

Children with sickle cell disease presenting to A&E should be admitted to Great Western ward. Discuss any queries with the Paediatric Haematology SpR or the on call Paediatric SpR. All admissions and attendance to A+E are discussed in the handover the following morning at 08.30 h. During working hours the Paediatric Haematology SpR should see children in casualty whenever possible.

Management is supportive unless there are indications for exchange transfusion (see page 28), which should first be discussed with a consultant paediatric haematologist. The aim of treatment is to break the vicious cycle of: sickling → hypoxia and acidosis → more sickling - all exacerbated by dehydration.

General management includes:

- analgesia
- giving reassurance that the patient's pain will be relieved as soon as possible
- massage and distraction techniques may help some children
- warmth; and establishing a position of maximum comfort
- hydration
- establish IV access as soon as possible
- identification and treatment of infection
- regular observations and reassessment
- all children receiving morphine must do incentive spirometry (see Appendix 8)

1. Analgesia

The painful crisis is the commonest cause of hospital admission, and needs to be addressed urgently. Pain in sickle cell disease may be very severe and is often underestimated by medical and nursing staff. First-line analgesia for severe pain is **a combination of intranasal diamorphine and oral morphine.** See also the Imperial Paediatric Sickle Cell Pain Management Protocol and Pain guidelines. **ALL** children admitted must have analgesia prescribed at regular intervals; a PRN basis is not recommended.

Codeine has recently been reported to cause severe respiratory depression and death in a small group of children who are fast metabolisers of the drug. Codeine should therefore only be used in patients who give a past history of codeine intake without any adverse effects. No codeine-naive patient should be prescribed the drug. If in doubt do not prescribe codeine. Please note that the NSAID of choice is ibuprofen, or alternatively, naproxen. Use of diclofenac in patients with sickle cell disease is discouraged due to concerns regarding its long term safety in patients with stroke and cardiovascular diseases.

An analgesic ladder is used according to the severity of pain and a pain tool must always be used to monitor effectiveness of pain relief.

morphine (oral + intranasal/ intravenous) + paracetamol + ibuprofen or naproxen

↑

paracetamol + ibuprofen or naproxen

↑

paracetamol/ibuprofen (if not already administered)

a) Moderate/Severe Pain

Please also refer to Imperial Paediatric Sickle Cell Pain Management Protocol: **Note below. Be aware this is a separate document from the Imperial paediatric pain guideline which should not be followed in this context.**

Intranasal diamorphine Intranasal diamorphine guideline

Age	Dose
All ages	0.1 mg/kg (maximum dose 6 mg)

Oral morphine – Doses from BNF for Children 2014-5

From age	To age	Dose
1 month	3 months	50 – 100 microgram/kg max. 4 hourly
3 months	6 months	100 – 150 microgram/kg max. 4 hourly
6 months	1 year	200 microgram/kg max. 4 hourly
1 year	2 years	200 – 300 microgram/kg max. 4 hourly
2 years	12 years	200 – 400 microgram/kg (max. 10mg) max. 4 hourly
12 years	18 years	10-15 mg max. 4 hourly

Stat i.v. bolus of morphine (if required) - once access established. This will take 5 - 20 mins to take effect. If necessary, repeat opiate (50 - 100% of initial dose after 20 mins.) Only to be given by doctors or anaesthetists or nurses trained in IV opioid pain relief.

From age	To age	Dose
1 year	12 years	100 micrograms/kg/dose
Over 12 years		5 -10 mg

If the patient remains distressed, discuss with SpR and/or pain team, consider intravenous infusion via PCA or NCA (see Appendix 1). Efficacy of analgesia should be assessed repeatedly over the first few hours and adjusted if necessary. Patients will vary in their analgesic requirements.

Morphine sulphate slow release tablets (MSTsr / Morphgesic SR)

Age	Dose
All ages	1 mg/kg bd maximum 70 mg/dose

For any patient receiving strong opiate analgesia, ensure PRN naloxone is prescribed as stated below:

Reversal of opioid-induced respiratory depression Naloxone

From	To	Dose
1 month	18 years	IV - 4 micrograms/kg, subsequent dose of 100 micrograms/kg if no response.

b) Mild/Moderate Pain

Please note that codeine is no longer used in children <12 year, codeine should only be used in children over 12 years of age who have had it before.

Dihydrocodine

From	To	Dose
4 Years	12 years	0.1 mg/kg (max 30 mg) 4 to 6 hourly
over 12 years		30 mg, 4 to 6 hourly, max. daily dose of 240 mg

Paracetamol, **oral** (over 1 month of age)

From	To	Dose
> 1 month of age	50 kg	18 mg/kg/dose 6 hourly (**maximum 75 mg/kg/day in 4 to 6 divided doses, up to a maximum of 4g in 24 hours)**
>50 kg		1 g 6 hourly (maximum of 4 g in 24 hours)

Paracetamol, **IV**

From	To	Dose
Term age	10 kg	10 mg/kg 6 hourly, regularly **(maximum 30mg/kg/day)**
10 kg	50 kg	15 mg/kg 6 hourly, regularly (**maximum 60 mg/kg/day in 4 divided doses)**
>50 kg		1 g 6 hourly **(maximum of 4g in 24 hours)**

Ibuprofen, oral

From	To	Dose
1 month	12 years	7.5-10 mg/kg/dose 6 to 8 hourly. (maximum 30mg/kg/day)
over 12 years		7.5-10 mg/kg/dose 6 - 8 hourly (maximum 600 mg 6 hourly)

Naproxen, oral
Note: there is no licensed liquid, round doses to 250mg or 500mg where possible, liquid is available in hospital but GPs will not prescribe, consider Ibuprofen

From	To	Dose
6 months	18 years	5 mg/kg twice daily maximum of 500 mg twice daily

Note: Dispersible diclofenac is no longer available.

2. Imperial Acute Pain Protocol for Management in A&E

EXCLUSION:

- Severe acute chest syndrome
- Girdle syndrome
- Vomiting

(Use morphine PCA instead - see separate protocol)

Assessed by A&E staff
Pain medication prescribed and given by A&E staff

Child attends A&E with sickle pain
Start protocol if <u>MAXIMUM DOSES OF</u> paracetamol and ibuprofen already given.

Give:
- Intranasal diamorphine 0.1mg/kg (max 6 mg) single dose *(See paediatric ED guideline)* **<u>AND</u>**
- Oral morphine liquid (Oramorph 10 mg in 5mL®) 400micrograms/kg (max 20mg)

First doses of analgesia should be given within 5-10 minutes of presentation to A&E
Prescribe:
- Regular **paracetamol** 18 mg/kg 6 hourly (8 hourly if under 3 months)
- Regular **ibuprofen** 7.5 mg/kg 6 hourly (If over 12 years can have 400 mg, do not use if under 1 month)

CALL PAEDIATRIC HAEMATOLOGY OR GENERAL PAED TEAM
Observations as below

Within 1 hour

Assessed by Paed Haem/ Gen Paeds

A second dose of oral morphine, 400 micrograms/kg should be given (maximum 20mg) **unless** there is respiratory depression or patient is pain free.

After a further 2 hours

Pain control unacceptabl

Morphine PCA (Bleep PSP for advice re setup- use standard paediatric proforma)

Pain control acceptable

Oral morphine liquid 400micrograms/kg (max 20mg) **(3rd dose)**

Pain control unacceptabl

Start **Morphine slow release tablets** (**MST SR/morphgesic SR)** 1 mg/kg BD (max 70 mg / dose) together with **oral morphine liquid** 400micrograms/kg (maximum 20 mg) PRN 3 hourly

Pain control acceptable

Continue **oral morphine liquid** 400 micrograms/kg (maximum 20mg) PRN 3 hourly

Note the available tablet sizes of slow release morphine are:

5mg, 10mg, 30mg. Please prescribe appropriately.

Note, if requested by child "Sevredol® tablets" (instant release morphine tablets) may be used instead of oral morphine liquid, ensure these are not confused with MSTsr® / morphgesic sr™ (slow release) tablets (both are controlled drugs)

- **Observations, Pain Assessment (scoring system)**
  - Hourly observations for first 24 hours, 2 hourly thereafter.
- **Dose Reduction**
  - Morphine slow release tablets dose can be reduced once oral liquid morphine requirements are < 4 doses in 24 hours.
  - Daily reduction of morphine slow release tablets 0.5 mg/kg BD, 0.25 mg/kg BD, stop.
- **Patients should not be discharged on morphine slow release tablets or Morphine Sulphate.**
- **Other medication** - The following should be routinely prescribed (refer to BNFC for dosage and Trust paediatric pain guidelines)
  - Constipation: Regular Movicol Paediatric or Movicol (age dependent).
  - Nausea: Ondansetron 100 micrograms/kg 8 hourly PRN (max 4 mg/dose) intravenous or intramuscular.
  - Reversal of opiate induced respiratory depression: Naloxone 4 micrograms/kg intravenous (intramuscular or subcutaneous injection if IV access not available - caution as onset of action delayed).
  - Morphine induced itch: Naloxone 0.5 micrograms/kg

3. Fluids

- Dehydration occurs readily in children with sickle cell disease due to impairment of renal concentrating power (hyposthenuria). Diarrhoea and vomiting are thus of particular concern.
- An IV line should be established whenever parenteral opiates have been given or if the patient is not taking oral fluids well.
- In the less ill patient who is able to drink the required amount, hydration can be given orally. As alternatives consider a nasogastric tube in an alert, co-operative patient.
- A fluid chart should be started and kept carefully, both input and output. Daily weight.
- The ill child should be assessed for the degree of dehydration by the history; the duration of the illness; by clinical examination; and (if known) weight loss. Haemoglobin and haematocrit may be elevated as compared with the child's steady state values.

Hyperhydration (150%) of normal requirements should be commenced on admission; **this must be reviewed on a daily basis. Caution if concomitant pneumonia as there may be inappropriate ADH secretion and hence normal maintenance could be more appropriate. This can be given IV or oral, depending on the child's ability to drink.**
These can be calculated in one of 2 ways:

(maximum total volume in 24 hours: 3 L in females, 3.75 L in males)

Either:	**3 L/m^2/24hours**	
Or:	**Body weight (kg)**	**Fluids (mL/kg/day)**
	Up to 10 kg	150 mL/kg/day
	11- 20 kg	1500 mL+ 75mL/kg/day for each kilo over 10 Kg
	>20 kg	2250mL + 30mL/ kg/day for each 1kg body weight over 20kg

For example:
An 8 kg infant will require 150 x 8 = 1200 mL per 24 hrs (50 mL/hr)
A 16 kg child will require (150 x 10) + (75 x 6) = 1950 mL per 24 hrs (81 mL/hr)
A 36 kg child will require (150 x 10) + (75 x 10) + (30 x16) = 2730 mL/24hrs (114 mL/hr)

Electrolytes should be reviewed, remembering that a slightly raised urea will often be significant as these children normally have a low blood urea.

Fluid type to prescribe should be 0.9% normal saline with 5% dextrose. Check U&Es at least daily and use KCl containing bags (10 mmol/L) as required.

4. Oxygen

This is of doubtful use if the patient has only limb pain, but may be given if requested by the patient. The patient's oxygen saturation (SaO_2) should be monitored by pulse oximetry with regular readings in air (minimum 4 hourly)

- If SaO_2 < 95% in air, give O_2 by face mask.
- Refer to patient's baseline oxygen saturations from clinic letters
- Monitor SaO_2 while patient is on supplementary O_2, aiming to keep SaO_2 > 98%.
- Check SaO_2 after a few minutes off O_2 on a daily basis, if clinically possible.
- If SaO_2 remains <95% in a child with normal baseline SaO_2, exclude emerging acute chest syndrome (ACS), see below.

5. Antibiotics

Infection is a common precipitating factor of painful or other types of sickle crises. These children are immunocompromised. Functional asplenia or hyposplenia occurs, irrespective of spleen size, resulting in an increased susceptibility to infection, in particular with capsulated organisms such as Pneumococcus, *Haemophilus influenzae* and *Salmonella* – all of which can cause life-threatening sepsis.

For painful crises where the patients do not need admission and there is no specific evidence of infection, prophylactic penicillin V may be increased from twice a day to four times a day until symptoms have settled.

- **For patients who are admitted with uncomplicated painful crisis without specific evidence of infection commence oral clarithromycin** (7 day course for children over 6 months of age), after cultures (blood, urine and any other source that is indicated) have been taken. An alternative is an oral cephalosporin (eg cefaclor, but not cefalexin). The rationale for these antibiotics is that they provide cover for Pneumococcus and Haemophilus without masking Salmonella osteomyelitis.
- If there are chest signs, or an abnormal CXR, give cefuroxime (iv) and clarithromycin.
- If there is abdominal pain and girdle syndrome is suspected, cefuroxime and metronidazole.
- If symptoms/signs of focal infection are present (e.g. tonsillitis, UTI) consult the hospital antibiotic policy for drug of choice.
- If the patient is unwell or fails to improve discuss with the paediatric infectious diseases team.
- **Stop prophylactic penicillin if any additional antibiotics cover Pneumococcus, such as clarithromycin and cefuroxime.**

Patients on desferrioxamine (DFO) who have diarrhoea should be started on ciprofloxacin immediately (after checking they are not G6PD deficient) and the DFO stopped. Ciprofloxacin can be stopped if Yersinia infection has been excluded. Use cefotaxime or ceftriaxone if patient G6PD deficient. Siblings of children with Salmonella infections should be discussed with the ID team.

6. Other Drugs

Please write up for:

a. Additional analgesia: if on oral/iv morphine should also have regular ibuprofen/naproxen and paracetamol prescribed.

b. Folic acid:

From	To	Dose
1 month	3 years	2.5 mg od
over 3 years		5 mg od

c. Anti-emetic: e.g. cyclizine (if receiving opiate analgesia)

From	To	Cyclizine Dose
2 years	5 years	0.5 - 1 mg/kg bolus dose oral/iv maximum 25 mg tds
6 years	18 years	0.5 - 1 mg/kg bolus dose oral/iv maximum 50 mg tds
		Can be given as an infusion

d. Laxatives, if receiving opiate analgesia (unless there are abdominal signs)

Macrogols sachets (e.g. Movicol paediatric or adult / Laxido)

From	To	Dose
1 month	1 year	Half to one sachet daily – *Movicol Paediatric*
1 year	6 years	1 sachet daily (adjusted to produce soft stools, max. 4 sachets/day) – *Movicol Paediatric*
6 years	12 years	2 sachets daily (adjusted to produce soft stools, max. 4 sachets/day) – *Movicol Paediatric*
12 years	18 years	1-2 sachets daily - *Movicol (Adult) / Laxido*

Lactulose

(NB Do not prescribe Macrogols AND lactulose concomitantly as both osmotic laxatives)

From	To	Dose (starting from)
1 month	1 year	2.5 mL 12 hrly dose adjusted according to response
1 year	5 years	5 mL 12 hrly dose adjusted according to response
5 years	10 years	10 mL 12 hrly dose adjusted according to response
10 years	18 years	15 mL 12 hrly dose adjusted according to response

Senna liquid (5 mL = 7.5 mg)

From	To	Dose (starting from)
1 month	2 years	0.5 mL/kg/dose nocte
2 years	6 years	2.5 - 5 mL nocte
6 years	12 years	5 - 10 mL nocte
over 12 years		10 - 20 mL nocte

e. Anti-pruritic (if receiving opiate analgesia)

Naloxone

From	To	Dose
1 month	18 years	IV – 0.5 micrograms/kg, repeat as necessary

Chlorphenamine (oral)

From	To	Dose (starting from)
1 month	2 years	1 mg 12 hourly
2 years	6 years	1 - 2 mg 4-6 hourly (maximum 6 mg/24 hrs)
6 years	12 years	2 mg 4-6 hourly (maximum 12 mg in 24 hrs)
over 12 years	12 years	4 mg 4-6 hourly (maximum 24 mg in 24 hrs)

Hydroxyzine

From	To	Dose
6 months	6 years	1 mg/kg or 5 - 15 mg initial daily dose at night increased if necessary to 50mg/day in 3 - 4 divided doses
6 years	12 years	1 mg/kg or 15 - 25 mg initial daily dose at night increased if necessary to 50-100mg/day in 3 - 4 divided doses
12 years	18 years	Initially 25mg daily dose at night, maximum dose of 100 mg/day in 3 - 4 divided doses

7. Pain at Particular Sites

a) Limb/Joint pain (including osteomyelitis): this is usually due to vaso-occlusive crisis but the possibility of osteomyelitis/septic arthritis needs to be considered. Management depends on index of suspicion and should be discussed with senior colleagues if in doubt. All patients should receive general supportive care as outlined on pages 12-14.

The diagnosis of osteomyelitis in the context of sickle cell disease is often difficult, and relies on factors such positive blood cultures, persistent local inflammation, unusual swelling and/or pain. Fevers may not be persistent. MRI scan of affected bone or joint must be undertaken as soon as possible, please discuss with the Consultant Paediatric Radiologist. Input from the orthopaedic team is valuable and need to be sought urgently. A high CRP may be helpful, but together with most of these other features may also occur in uncomplicated vaso-occlusive crisis. Note that X-ray changes do not appear until about 10 days after the onset of infection. Joint aspiration may be useful in order to try to identify organisms if fluid has been seen on ultrasound. Note that the fluid can be quite purulent even in patients with sterile infarcts.

Salmonella is the commonest organism in osteomyelitis in sickle cell patients, but *Staphylococcus* and *S. pneumoniae* are also common. If the decision is taken to treat for osteomyelitis antibiotics should be chosen to cover these organisms. A useful regimen is intravenous ceftriaxone and clindamycin, but the advice of the infectious diseases team should usually be sought. Decisions over the length of treatment will depend on the certainty of diagnosis and clinical course, and will usually involve input from the orthopaedic and infectious diseases teams.

Never aspirate an affected joint without prior discussion with a consultant paediatric haematologist.

b) Abdominal pain: see page 16.

c) Chest Pain: see page 17.

MANAGEMENT OF SPECIFIC SICKLING PROBLEMS

1. Abdominal Crisis & Girdle Syndrome

Abdominal crises often start insidiously with non-specific abdominal pain, anorexia and abdominal distension. As abdominal pain is not an infrequent symptom in children, the differential diagnosis may be difficult. Constipation may often co-exist, especially if codeine or other opiates have been used as analgesia. In an abdominal crisis, bowel sounds are diminished, and there is often generalised abdominal tenderness; rebound tenderness is absent. The abdomen is not rigid and moves on respiration. Vomiting and diarrhoea are usually not prominent features.

Girdle (or mesenteric) syndrome is characterized by an established ileus, with vomiting, a silent distended abdomen and distended bowel loops and fluid levels on abdominal x-ray. Some hepatic enlargement is common, and it is often associated with bilateral basal lung consolidation (chest syndrome).

Differential Diagnosis
Consider the possibility of acute appendicitis, pancreatitis, cholecystitis, biliary colic, splenic abscess, ischaemic colitis and peptic ulcer. Well localised or rebound tenderness and/or board-like rigidity or lack of movement on respiration are suggestive of these diagnoses. Ultrasound may be helpful. If surgical intervention is contemplated, exchange transfusion should be performed prior to laparotomy: this may need to be started pending clarification of the diagnosis.

Investigations

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

Management

In addition to analgesia and fluids, as outlined before:

- If there is vomiting, abdominal distension or absent bowel sounds, give nothing by mouth and consider nasogastric suction.
- Request paediatric surgical review
- Monitor abdominal girth (at umbilicus) 1-4 hourly; measure liver size bd.
- Examine chest. Monitor SaO_2 in air.
- If SaO_2 in air <90%, as per chest syndrome (page 17)
- Antibiotics: If patient is pyrexial and/or unwell first line is cefuroxime plus metronidazole. If unusual features discuss with ID Team.

Girdle syndrome is an indication for exchange transfusion.

2. Acute Chest Syndrome (ACS)

Acute sickle chest syndrome is likely to be multifactorial in origin with infection, thrombosis of pulmonary arteries and fat embolism all resulting in potentially similar clinical patterns. Regular observations, careful opiate administration and pulse oximetry recorded in air are important in recognition of this complication.

Symptoms

- May develop during a painful vaso-occlusive limb crisis and often presents a few days into the admission.
- Pain (often pleuritic) in chest wall, upper abdomen and/or thoracic spine. May present as abdominal pain
- Dyspnoea
- Cough may be a late symptom.

Signs

- High fever, tachypnoea, tachycardia.
- Signs of lung consolidation, usually bilateral, generally starting at the bases, but may be unilateral and impossible to distinguish from infection.
- Bronchial breathing may be very striking. Physical signs often precede x-ray changes.

Differential diagnosis.

Sickle lung and pneumonia can be 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 subdiaphragmatic inflammation.

Investigations

- Venous blood gas to exclude acidosis
- Chest x-ray
- Blood, throat & sputum cultures and respiratory infection serology (Mycoplasma, Legionella, viral)
- Group & Save, make sure phenotyped red cells are available for transfusion; if diagnosis of ACS clear, blood should be x-matched for exchange transfusion.

Management

- **Transfer all unstable patients to HDU**
- **Oxygenation** - Options include face mask oxygen, CPAP, CNEP, Optiflow, ventilation, and the use of exchange transfusion. Early involvement of consultant/SpR is essential. Have a low threshold for using CPAP/CNEP/Optiflow if there are chest symptoms and O_2 saturations <95%. A worsening chest x-ray, rapid fall in O_2 saturations or persistent fever may all be indications for exchange transfusion.
- **Intravenous fluids with hyperhydration**, as for painful sickle crisis.
- **Antibiotics:** IV cefuroxime and oral clarithromycin bd. (Stop prophylactic penicillin V).
- **Incentive spirometry** device in conjunction with the physiotherapist
- **Monitor** oximetry on air & blood gases as indicated, pulse & respiratory rate.
- ***NB*** Diuretics are **contraindicated** even though chest x-ray and/or signs may mimic pulmonary oedema.
- Bronchodilators: may be useful for those patients with known airways disease but should not be used routinely. (Cochrane Database Syst Rev. CD 003733, 2012: insufficient evidence for routine use).

3. Aplastic Crisis

Transient 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. The main differential diagnosis is splenic sequestration but in this reticulocytes are high and jaundice is often prominent and there is splenomegaly. Aplastic crisis may affect multiple members of a family concurrently or consecutively. Second infections with Parvovirus are extremely rare as immunity to parvovirus is life-long.

Diagnosis

- Hb >20 g/l below steady state level or rapidly falling Hb.
- Reticulocytopenia, absence of polychromasia and nucleated red blood cells on blood film despite low Hb.
- Parvovirus IgM present.

Management

- Urgent red cell transfusion is often necessary (if Hb <50 g/L and/or symptomatic)
- Spontaneous recovery is heralded by return of nucleated RBCs and reticulocytes to peripheral blood

STROKE AND OTHER CNS MANIFESTATIONS

1. Stroke

Stroke is a potentially devastating complication of sickle cell disease, most commonly occurring in individuals with homozygous disease (HbSS) or HbS$\square^0$. Vaso-occlusion of the cerebral vessels leads to infarction, generally in the territory of the middle cerebral artery, and untreated the majority will have a recurrence. Predictive factors for stroke include those with a history of transient ischaemic attacks, chest syndrome, hypertension, or those with a low Hb F and/or a low total haemoglobin. The Stroke Prevention Trial (STOP) showed that children with trans-cranial Doppler (TCD) velocities of >200 cm/s are also at significant risk.

Investigations

- MRI/CT scan of brain without contrast should be performed to look for CVA and to exclude haemorrhage (infarcts may not be apparent on CT in the very early stages).
- MR angiography should be performed later (see below).
- Before transfusing, take blood for: ferritin, LFTs, red cell phenotyping, serology for HIV, CMV, and Hepatitis B & C infection (if these not already done).

Lumbar puncture may be necessary to exclude infection or subarachnoid haemorrhage.

Management

- Rehydrate immediately
- Urgent neurological assessment, and regular monitoring of neurological status
- Seizures may occur and require anticonvulsant therapy
- If clinically unstable, exchange transfusion must be carried out urgently; this should be done preferably by automated erythrocytapheresis or if unavailable, by manual exchange transfusion performed in 2 or 3 stages with an interval of 4-8 hours between each exchange. The aim is to achieve a HbS level below 20%.
- If clinically stable exchange transfusion should also be carried out urgently whenever possible and children should be transfused to 100 g/L until such time; the decision about the timing of exchange transfusion will need to be made for each individual patient depending upon all considerations including past history and ease of venous access; such cases should all be discussed with the Paediatric Haematology consultant on call.
- Children with **T**ransient **I**schaemic **A**ttacks: Unless the child is clinically unstable, it is not usually necessary to exchange transfuse urgently 'out of hours'; the decision for exchange transfusion should be taken only where there is evidence that there is a new infarct or bleed and/or the child is clinically unstable. Discuss need for exchange transfusion with the paediatric haematology consultant on call.

Non-urgent management:

- MR angiography (to assess the pathogenesis, risk of recurrence and need for revascularisation) - the risk of recurrent neurological events is greatest in those with abnormal cerebral vasculature.
- Trans-cranial Doppler studies
- Establish a monthly transfusion programme to maintain the HbS level <30% for first event and <20% for subsequent events or evidence of progressive vasculopathy.

2. Stroke Prevention

Transcranial Doppler imaging (TCDi)

TCD ultrasound imaging assessment (TCDi) is a non-invasive method of identifying children at risk of ischaemic stroke. Annual assessments are recommended in children with SCD and SB0 thalassemia from the age of 2 until at least 16 years . In children with other genotypes (SB+ thalassemia and HbSC), TCD is not recommended as a standard of care and should be reviewed on a case by case basis.

TCDi is performed by specialist trained vascular scientists at the Irvine Vascular Lab at St Mary's Hospital and is generally arranged to coincide with clinic visits.

TCDi is defined by Time average maximal mean velocity (TAMM) in the inferior, middle and posterior cerebral arteries (ICA, MCA & PCA respectively).

TAMM blood velocities used as cut-offs to define at risk limits for TCDi as per UK National TCD guidelines (2010) are outlined below. These results are adapted from criteria derived from the first Stroke Prevention Trial in Sickle cell Anaemia (STOP1 trial) where non-imaging TCD scanning was used.

Normal velocity "standard risk"	< 155cm/s
Borderline velocity "conditional risk"	155 – 179cm/s
High velocity "high risk"	> 180cm/s

A TCD is defined as "inadequate" if unsatisfactory results are obtained. This can occur if the patient is uncooperative or if visualizing the vessels via the bony window is not possible. In this context a repeat scan should be attempted or an alternative scanning method, such as MRI/MRA should be considered.

"Conditional risk" results warrant repeat TCD scanning – the interval chosen to perform these scans is defined on an individual case basis. "High risk" scans demand the need for urgent MRI/MRA imaging to further define the extent of cerebrovascular disease. The stroke risk is up to 30-40% in those in the "high risk" category and in these cases long-term regular transfusion programmes to reduce this risk should be considered.

Trans-Cranial Doppler Ultrasound Guidelines (Paediatric Services Only) "Guidelines on Trans-Cranial Doppler ultrasound should be in use covering at least:

a) Subarachnoid Haemorrhage

Uncommon in children but beware of teenagers, and often associated with multiple intracranial aneurysms.

Investigation

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

Management

- Exchange transfusion should be arranged urgently as re-bleeds may occur and/or surgery be advised. Refer to neurosurgeons.

b) Convulsions

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, and may occur following administration of intravenous pethidine.

Investigations

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

Management

Immediate

- Anticonvulsant, usually IV lorazepam, buccal midazolam, or rectal diazepam, as per status epilepticus guidelines. Status epilepticus Guidelines
- Antipyretic, such as paracetamol
- Unless likely to be a febrile convulsion or the child is known to be epileptic, an urgent CT scan should be performed
- Discuss need for exchange transfusion with paediatric haematology consultant on call. Unless the child is clinically unstable, it is not usually necessary to exchange transfuse urgently 'out of hours'; the decision for exchange transfusion should be taken only where there is evidence that the seizures are associated with a new infarct or bleed and/or the child is clinically unstable.

Definitive

- If no abnormality on EEG and CT/MRI, and no recurrence, watch and wait.
- If EEG abnormal, but CT/MRI and MR angiography are both normal, consider anticonvulsants.
- If infarction on scanning, or vessel stenosis/occlusion on angiogram, exchange transfuse and consider hypertransfusion regimen for ≥36 months.

SEQUESTRATION SYNDROMES

1. Splenic Sequestration

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

Symptoms

- Abdominal pain (pulling legs up to abdomen)
- Abdominal distension
- Maybe sudden collapse

Signs

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

Investigations

- FBC & reticulocytes (raised in sequestration, absent in aplastic crisis)
- Blood cultures & other infection screen, as clinically indicated
- Parvovirus B19 serology (differential diagnosis is aplastic crisis)
- Cross match half the patient's estimated blood volume immediately

Management

- Resuscitation with fluids.
- Emergency top-up transfusion, if necessary with O Rh -ve ('flying squad') blood
- Broad spectrum antibiotics such as cefuroxime
- Before discharge, teach parents to recognise the symptoms and to detect an increase in spleen size
- Consider a hypertransfusion regimen until maximum reduction of spleen size
- Consider splenectomy if recurrent (>1 episode)

2. Hepatic Sequestration

Symptoms

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

Signs

- Enlarging tender liver, increasing jaundice
- Collapse/shock is less common than with splenic sequestration but can occur

Investigations

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

Management

- May need urgent top-up transfusion
- IV cefuroxime.
- If the patient becomes tachypnoeic, or develops chest signs, then check arterial blood gases and treat for sickle chest syndrome

TRANSFER TO PICU/HDU

Children having progressive organ failure or requiring an emergency exchange transfusion or who are unstable in any other way require transfer to HDU where they will be jointly managed by the Paediatric Haematology and HDU/PICU teams.

It is important to discuss any patient likely to require HDU/ PICU admission as early as possible with the PICU team. Patients will be considered for admission to PICU for invasive monitoring and therapy of the following:

- a compromised airway
- actual or impending respiratory failure
- hypotension requiring inotropic support
- sepsis syndrome
- renal failure likely to require dialysis/haemofiltration
- may need transfer for insertion of adequate access for exchange transfusion

EXCHANGE TRANSFUSION

Whenever possible, exchange transfusions will be undertaken by automated erythrocytapheresis by suitably trained nursing staff. This allows for safer, euvolemic and full-volume exchanges in a much quicker timescale compared to manual exchanges. Manual exchanges, however, may need to be undertaken out of hours, when trained staff are not available for automated exchanges or if suitable IV access is not secured.

The following applies to **manual exchanges only**. For further information regarding automated exchanges, please refer to SOP for automated exchange transfusions or contact the Haemoglobinopathy CNS.

Exchange transfusion is undertaken to rapidly reduce the percentage of sickle cells in the circulation when a patient develops a life-threatening complication of the disease. It is not to be undertaken lightly, as the possible complications are considerable. However, patients with the following problems justify the risks:

- Severe chest syndrome (e.g. low or falling PaO_2) or girdle syndrome
- A new CVA
- Multi-organ failure, e.g. associated with systemic fat embolism
- Fulminant priapism (> 4 hours) unresponsive to pharmacological therapy (as impotence can be the long-term outcome)

Exchange transfusions should only be undertaken under the supervision of experienced medical and nursing staff and in an emergency situation and should not be initiated without discussion with the responsible consultant. The red cells used should be specially grouped (ABO compatible, Rh negative (rr) or R_O as appropriate, Kell compatible), and HbS negative. Ensure the Blood Transfusion Laboratory is aware that the blood required is for exchange transfusion.

Aim

a) To reduce the HbS level to <20% over 2 - 3 days unless acutely ill, when more rapid exchange may be appropriate
b) To keep Hb $\leq$100 g/L initially and by the end of the whole procedure (or at steady state level in those with higher baseline Hb, e.g. HbSC patients ≈110-120 g/L).
c) To maintain a steady state blood volume and Hb throughout the exchange

- Use SAG-M blood, which is the freshest available (to prolong its life in the patient).
- Do not use diuretics.
- Continue to administer IV fluids at hypertransfusion rate between transfusions.

If manual exchange is being used, critically ill patients may require them more frequent than daily for rapid reduction of sickle percentages. Where possible, leave a 4 - 8 hour break between manual exchanges. For patients undergoing exchanges, particular attention should be paid to PaO_2, CVP, venous gas, U&E, bone profile, temperature and clotting.

Preliminary investigations

- FBC
- HPLC
- Extended RBC phenotype (if not already known), x-match.
- U&E, bone profile (particularly calcium)
- Venous blood gases - in those with symptoms suggestive of acute chest or girdle syndrome,
- Serology for Hepatitis B & C, if not done recently.

Volumes required
The number and volume of exchange transfusions performed in a child with sickle cell disease will depend on the severity of the clinical problem and the haemodynamic stability of the child

A 'total' exchange is 1.5 - 2 times the child's blood volume and this is usually performed in 3 or 4 exchange procedures

Volume (mL) of blood removed *for each procedure* should be:

30 x weight (in kg) = volume in mL,

Preparation of the patient
Patients must be well hydrated prior to starting an exchange transfusion. Adequate explanation must be given to the child and parents as to the indication for exchange and its potential risks and benefits and this should be documented in the case-notes.

Venous access
Two ports of venous access are required; one for venesection, the other for administering blood and crystalloid; in certain circumstances, an arterial line may be used for venesection.

Procedure

- **The aim is that this should be an isovolaemic procedure with monitoring of blood pressure, heart rate and oxygen saturations every 15 minutes, and 1 hourly temperature monitoring**. Exchanges are done in 'aliquots' of approximately 1/10 of the total to be exchanged (never greater than 5% of the blood volume). Note that the haematocrit of transfused packed cells (approximately 0.5-0.7) is higher than that of the venesected blood.

- **It is important to ensure that the child is well hydrated between successive exchanges and that the haemoglobin is regularly monitored and kept at or below 100 g/L at all times.**

- **For the first procedure**, start by venesecting 30% of the above volume (ie approx 10 mL/kg) in aliquots of 10 - 50 mL every 15 minutes using a large syringe. Normal saline should be concurrently infused at the same rate to maintain isovolaemia. If the child has haemoglobin of less than 60 g/L replacement with blood rather than normal saline will be needed. *It is essential to ensure that blood is ready and easily available from Blood Bank before commencing.*

- The venesected blood can be discarded into a venesection bag via a 3-way tap. Venesection bags are kept on PHD unit and Grand Union.

- Continue venesecting the remaining two thirds of the volume (20 mL/kg) in aliquots of 10 - 50 mL (approximately 1/10 of total exchange) every 15 minutes replacing with blood at the same rate (approximately 12 mL/kg/h, red cells in SAG-M) instead of normal saline. This process should take no more than 120 min, depending on the rate of flow of blood and the clinical condition of the patient.

- Where possible leave at least 4-6 hours between each exchange procedure (very 30 to 40 mL/kg). In critically ill patients exchanges may need to be continuous.

- Check FBC, HPLC, U&E, LFT, bone profile and clotting, at the end of each 10 mL/kg. Ensure that the Hb $\leq$100 g/L to reduce the risk of hyperviscosity.

- Continue with 3 to 4 exchange procedures until the Hb S <20%.

- **NB For the second and subsequent exchange procedures, it may be necessary to use a ratio of 50% saline: 50% blood (rather than 30:70) in order to prevent the Hb from rising too high. This should be discussed with the paediatric haematology SpR or consultant when planning the procedure.**

- A top-up transfusion can be given at the end of the final exchange procedure to give a final Hb of 100 g/L.

Possible immediate complications

- Urticarial reactions or angioedema due to HLA antibodies. Treat with antihistamine and/or corticosteroid
- Metabolic disturbances are rare, occurring usually in small children, or in association with visceral sequestration requiring continuous exchange.
- Convulsions are very rare. They are usually a sign of cerebral sludging, often in patients with previous CNS problems. Check that Hb has not risen too high (>110 g/L). Give anti-epileptics; ensure there is a large fluid intake; give oxygen.
- Hypertension is occasionally seen in patients with circulatory overload. If diastolic BP increases by >20 mmHg, slow down exchange, check Hb not >110 g/L or hct not >0.4. If diastolic BP is > 100 mmHg stop the exchange, venesect, and consider antihypertensives.

ELECTIVE TRANSFUSIONS

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 level below 25%. This can be achieved by regular top-up (or additive) transfusions keeping the Hb between 100 and 140 g/l, as in patients with □-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 better venous access.

Elective transfusions can also be performed on an ad hoc basis for Sickle Cell patients undergoing elective surgery (with the intention of achieving a Hb of 100g/L) Please refer to 3.18 for more information.

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

- FBC
- HbS level
- Antibody screen & crossmatch
- U&Es, LFTs
- Ferritin

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 in g/L$_{desired}$ – Hb in g/L $_{current}$) x weight (kg) x 4

Do not attempt to raise the haemoglobin by more than 40 g/l at any one transfusion.
The usual rate of transfusion is **5mL/kg/hour** and for elective transfusion should **never exceed a maximum rate of 150 mL/kg/hour**.

Post-transfusion, check FBC and HbS level.

Top up transfusions are generally performed monthly; if the pre-transfusion Hb is < 100 g/l, more frequent transfusions are required. If the post-transfusion Hb is < 130 g/l, insufficient blood is being given. In some cases failure to get an adequate increment may be due to an enlarged spleen resulting in hypersplenism.

Investigations to be performed

- HBsAg, level of anti-HBs Ab (revaccinate if < 100 iu/mL) annually. Remember to state on the virology request form that the patient has been vaccinated.
- HCV Ab and save serum annually
- HIV Ab (with parental/guardian consent) at outset.

TRANSFUSION REACTIONS

Intravascular haemolysis: usually presents within minutes of starting the transfusion and may be an indication of blood group incompatibility.

- Discontinue the transfusion immediately,
- Check ABO of blood against patient's blood group
- Ensure adequate hydration
- Inform the haematology SpR and Blood Transfusion Laboratory.
- Monitor for renal dysfunction and haemoglobinuria by urinalysis and measuring urine output.

Non-haemolytic, febrile reactions: occurring an hour or more after commencing the transfusion, often indicate sensitisation to plasma proteins or white cells. Initially slowing the rate of transfusion and administering chlorphenamine +/or hydrocortisone may help. If pyrexia persists or the patient is clinically unwell discontinue the transfusion.

Pyrexia associated with rigors (but not hypotension) occurring more than one hour after starting the transfusion usually indicates alloimmunisation - antibodies to Rhesus or other blood group antigens, the transfusion should be discontinued. Paracetamol and/or chlorphenamine should be given. Discuss with haematology SpR and Blood Transfusion Laboratory and investigate appropriately following discussion.

See St Mary's / Imperial NHS Trust Blood Transfusion Guidelines for Children and Neonates for transfusion administration and management of adverse events.

IRON OVERLOAD AND CHELATION THERAPY

Deferasirox (DFX) is the chelator of choice in children > 2 years of age on regular transfusions who have evidence of organ iron overload. **Chelation therapy should usually commence after a child has received 15 transfusions or when the ferritin reaches 1000 μg/l**. However as ferritin is an acute phase reactant which rises with acute infection or inflammation, it is important that the ferritin is checked at least on 2 occasions when the patient is well, prior to starting chelation therapy. The decision to start chelation therapy must be discussed with a Paediatric Haematology Consultant beforehand.
DFX may cause hepatic or renal dysfunction. Ensure creatinine and hepatic transaminases are normal prior to commencement of therapy. Baseline ophthalmology and audiology monitoring is necessary prior to starting treatment and yearly thereafter. Monitor serum biochemistry and full blood count fortnightly for 1 month when starting treatment and at every dose escalation, and then monthly for the duration of therapy. .
DFX is started at 15mg/kg/day orally, rounded up to nearest available tablet sizing; 125mg, 250mg and 500mg tablets are available. Tablets should be dispersed in water or orange juice prior to intake. Increase doses every 3-6 months at 5-10mg/kg steps**, aiming to reach a dose of 30mg/kg**. Ensure that compliance is adequate before dose increases to >30mg/kg. **Never exceed a dose of 40mg/kg as higher doses are significantly associated with hepatic and renal dysfunction**. Discuss with the patient's named consultant prior to increasing chelation doses.

Desferrioxamine (DFO) may also be used in children who are intolerant to DFX. Desferrioxamine has a detrimental effect on skeletal growth and treatment should be deferred until the age of 2 years unless iron overload is particularly severe. For those on regular top-up transfusions with a rising ferritin, desferrioxamine (DFO) is usually given as an overnight subcutaneous infusion. **The standard dose of DFO is 25 - 40 mg/kg/day up to 7 nights per week.** Local reactions and severe allergy may occur at DFO infusion site. **Vitamin C at a dose of 2 mg/kg/day (maximum 100 mg/day)** should be given on the days when the patient receives DFO. This should not be commenced until the patient has been on DFO for one month. It should not be given to patients with cardiac dysfunction.

The other available oral iron chelator is Deferiprone (DFP). The use of DFP in children with Sickle Cell Disease who have iron overload due to chronic transfusions has not been fully investigated and clinical trials are currently under way. At present DFP is not used in children with Sickle Cell Disease.
.
Iron chelation must be stopped and the patient admitted for investigation and treatment if they develop abdominal pain & diarrhoea as this may be due to Yersinia infection.

Investigations prior to starting and on Chelation

- Annual ophthalmology review (including baseline)
- Annual audiology review (including baseline)
- Glu, HbA_{1C}, cortisol,
- TSH/T_4, FSH/LH/oestradiol or testosterone,
- ECG & ECHO or MUGA-scan
- Monitor growth including sitting and standing heights (see also growth and endocrine section)
- MRI for estimate of liver/cardiac iron overload at intervals depending on compliance.

PRIAPISM

Priapism (painful penile erections) can occur in childhood, and is often under-reported. It often starts at night in association with a full bladder. Untreated it can cause cumulative damage and may result in impotence later.

Types of presentation

- **Acute, fulminant** (> 4 hours).
- **Stuttering** (repeated painful erections lasting more than 30 minutes)

Management of acute/fulminant priapism

- Rehydrate immediately
- Opiate analgesia, +/- sedation
- Catheterisation, if necessary, to empty bladder
- Paediatric Haematology team to plan emergency red cell exchange transfusion
- Urgent Paediatric urology opinion (as per the trust Paediatric Surgery referral pathways)

Management of stuttering priapism

- Increased oral fluids, with frequent emptying of bladder
- Oral analgesia
- Drug treatments such as Anti-androgens (cyproterone), α-agonists (etilefrine) or oestrogens (diethyl stilbestrol) can be used in the short to medium term (on the advice of the Paediatric Urologists) to prevent spontaneous erections.
- Consider exchange transfusion followed by a period of hypertransfusion

The patient should seek medical attention if an episode lasts > 3 hours.

RENAL PROBLEMS

1. Haematuria

Microscopic haematuria is common in sickle cell disease; macroscopic haematuria may be due to urinary infection or papillary necrosis. Passing of renal papillae may cause renal colic and ureteric blockage. Haematuria can also occur in patients with sickle trait.

Investigation

- MSU for culture to exclude infection
- Ultrasound scan
- Hydrated intravenous urography may be necessary to establish the diagnosis, discuss with registrar or consultant first.

2. Albuminuria and Proteinuria

Albuminuria and proteinuria are not uncommon in children with sickle cell disease and may reflect underlying renal damage due to Sickle Cell Disease. It is very important to undertake urinalysis in children over 10 years at every clinic visit and to quantify urinary protein –creatinine ratio in children with 1+ or higher protein on urinalysis. Ensure urinary tract infection (UTI) is excluded. Persistent proteinuria requires further investigation. Please discuss with Paediatric Haematology Consultant and Paediatric Renal Consultant.

3. Urinary Tract Infections

Not uncommon in sickle cell disease, in both sexes. It should be vigorously investigated and treated to prevent serious renal pathology. Haematuria, secondary to papillary necrosis, can precipitate UTI, but other factors must be excluded. Any child with a UTI should be treated and then investigated according to RCPCH guidelines.

4. Chronic Renal Failure

Uncommon in children. Predictors include increasingly severe anaemia, hypertension, proteinuria, the nephrotic syndrome, and microscopic haematuria.

Investigations

- Urea and electrolytes, calcium, phosphate, bicarbonate; immunoglobulins and autoantibodies.
- FBC and reticulocytes
- MSU for M,C & S; 24 hour urine collections for protein and creatinine clearance
- Ultrasound of kidneys and urinary tract

Management

- Refer to Paediatric Renal Consultant
- Consider erythropoietin and/or hypertransfusion regime

EYE PROBLEMS

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. Vitreous haemorrhage and retinal detachment may occur in patients with HbSC disease. Thus these children require annual ophthalmological assessment from puberty onwards. Also children on regular transfusion regimens receiving desferrioxamine or deferasirox require annual ophthalmological assessment.

Management

- Refer to the Paediatric Ophthalmology Consultant
- Laser therapy is the treatment of choice for proliferative sickle retinopathy.
- Surgical treatment should not be undertaken without prior exchange transfusion.
- The service has a established referral pathway to the Western Eye

THE BILIARY TRACT

1. Gallstones

Pigment gallstones due to ongoing haemolysis is common in sickle cell disease, occurring in at least 30% of children. It is often asymptomatic but can precipitate painful abdominal crises and the girdle syndrome. It can also cause:

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

Investigations

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

Differential diagnosis of Right Upper Quadrant (RUQ) abdominal pain

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

Management

Acute episode of cholecystitis

- Analgesia
- Hydration
- Antibiotics

Recurrent episodes of cholecystitis

- Indication for cholecystectomy

Common bile duct obstruction (Acute)

- Endoscopic retrograde cholangiopancreatography (ERCP) *or* emergency surgery.

Common bile duct obstruction (Sub-acute)
After one attack, refer for surgical opinion regarding elective cholecystectomy; generally undertaken laparoscopically.

2. Intrahepatic Cholestasis

Some patients experience episodes of severe hyperbilirubinaemia (conjugated + unconjugated) with moderately raised alkaline phosphatase, associated with fever and hepatic pain in the absence of demonstrable stones. These episodes are thought to be due to severe intrahepatic sickling.

Management

- 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

AVASCULAR NECROSIS OF HIPS AND SHOULDERS

This complication may start in adolescence and often gives rise to chronic pain and limitation of movement due to joint damage, rather than ongoing vaso-occlusion

Presentation

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

Differential diagnosis

- Osteomyelitis
- Septic arthritis
- These are suggested by swinging pyrexia, severe systemic disorder, positive blood cultures and toxic granulation in neutrophils

Investigations

- X-ray
- MRI (This will usually show changes earlier than x-ray)
- Isotope bone scan can be very difficult to interpret in the presence of active sickling.

Management

- Analgesia as per the protocol
- Stop if Child is on Hydroxycaramide
- Rest and the avoidance of weight bearing (v. difficult to implement).
- 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.

GROWTH, PUBERTY AND FERTILITY

1. Delayed Puberty

Common, particularly in boys.
Related to lower body mass for age in children with sickle cell disease.
Reassure, as most will progress to puberty and achieve normal height despite the delay.

Management

- In the very thin patient, attempt to improve the appetite and quality of nutrition in order to increase the body weight.
- If an endocrine review is appropriate, or replacement therapy needed then refer to Dr Nicola Bridges, Paediatric Endocrinologist - 3 monthly clinic at St Mary's
- Regular transfusion for 6 - 12 months almost always initiates puberty delayed due to sickle cell disease
  (Exceptionally, infarcts in the hypophysis and hypothalamus are responsible)

2. Fertility

Girls are normally fertile, whereas many boys with HbSS and S□°-thalassaemia have reduced sperm counts and reduced sperm motility - some may have erectile impotence because of past priapism.

For information about pregnancy, contraception and termination of pregnancy discuss with the Paediatric Haematology Consultant and refer to adult guidelines.

3. Children with Sickle Cell Disease but not on Regular Transfusions

Most of these patients will not need endocrine follow-up

Measurements
Height should be measured and plotted at least yearly. Sitting height measurements should be recorded if the child is likely to start regular transfusions, if there are spinal crises in sickle cell anaemia, or there is concern about low bone density.

Puberty
There is an increased risk of pubertal delay. Pubertal development should be monitored.
Refer if there are no signs of puberty by 13 years in a girl or 14 years in a boy, it may be appropriate to refer earlier if there are psychological issues related to delay.

Blood tests
Regular Vitamin D monitoring
If growth velocity is poor or the child is unexpectedly short for parents, check thyroid function, coeliac screen, karyotype in girls.

Bone age and scans
Radiological assessment of bone age is indicated if growth velocity is poor or if the child is unexpectedly short compared to the parents. Pelvic U/S Ultrasound is useful as a baseline in girls with pubertal delay and in monitoring the progress of treatment.

Bone Mass Densitometry measurements
Consider at age 10 if there are concerns, all should have Bone Mass Densitometry (BMD) at the end of pubertal growth. There is an increased risk of low BMD in this group.

Further investigations
Not unless indicated

4. Children on Regular Transfusions

Should have regular endocrine monitoring because of the risk of problems related to transfusions and desferrioxamine. Desferrioxamine can cause bone abnormalities and reduced spinal growth.

Measurements
Height at least yearly to 10 years of age, and then every 6 months.
Sitting height at each visit.

Puberty
Puberty may be delayed or fail to occur at all. The commonest pituitary abnormality related to iron deposition is gonadotrophin deficiency. Pubertal development should be monitored.

Puberty is delayed if there are no signs of puberty by 13 years in a girl or 14 years in a boy, however if pubertal delay is likely treatment should start before this.

Blood tests

Once yearly after age 7:

- Thyroid function
- Calcium and bone profile
- Random or fasting glucose
- Electrolytes
- LFTs

Once yearly after age 10:

- Oral Glucose Tolerance Test: *if there are clinical concerns about adrenal function*
- Synacthen test
- LH/FSH
- Estradiol or testosterone

Bone age and scans

- Bone age every 2 years after age 4 or when starting desferrioxamine.
- Spinal x-rays should be considered if growth is disproportionate in patients on desferrioxamine.
- Pelvic ultrasound is useful as a baseline in girls with pubertal delay and in monitoring the progress of treatment.

BMD measurements
BMD measurement at 10 years and at the end of puberty.
Check yearly if the BMD is abnormal (i.e. in the osteopaenic or osteoporotic range).

Further investigations

- GH testing needed if growth velocity is poor.
- GnRH test may help in defining gonadotrophin status.
- Gonadotrophin status may need rechecking at the end of growth. Some patients will require long term sex steroid supplements.

SURGERY AND ANAESTHESIA

1. Peri-operative Management Plan in Sickle Cell Disease

Children with sickle cell disease are at a high risk of complications and serious adverse events (SAE) related to their underlying condition during the peri-operative period, regardless of the operative risk of the procedure itself.
The peri-operative management of patients with sickle cell disease requires good communication at all times between the surgeons, anaesthetists, haematologists, paediatricians and nursing staff. It is essential that the paediatric haematology team be informed well in advance so that they can help to formulate an appropriate management plan; they should have >2 weeks' notice of elective surgery in case plans need to be made for exchange transfusion. Children undergoing splenectomy require additional vaccinations to protect from infection with encapsulated bacteria; please see Appendix 2 for further details.

2. Pre-op Clinic

- Ensure that the red cell phenotype is known by the blood transfusion laboratory. **In all cases there must be phenotyped blood cross-matched before surgery.**
- Ensure that there is a plan from the paediatric haematology team for the peri-operative management of the patient. In addition if the patient is referred from another hospital, it is essential that there is also discussion with the haematologists from that hospital to ensure that the relevant past history is communicated and that there is a joint peri-operative management plan.
- Complete the pre-operative checklist and leave in front of patient notes (See Appendix 12 or the Source for checklist)
- Ensure that the Paediatric Haemoglobinopathy CNS has been informed.
- Ensure that the anaesthetists have been informed.
- Ensure that any special support e.g. PICU/HDU bed for CPAP has been organised.

3. Pre-op Transfusion

A recent UK-led multi-centre, randomised control trial of patients with HbSS and HbSβ0 thalassaemia looked at the benefit of pre-operative transfusion in low and medium risk surgeries (TAPS study, Lancet 2013; 381: 930–38). The incidence of SAEs (mainly chest crisis) were significantly higher in the non-transfused group; leading to the trial closing early and the investigators concluding that pre-operative transfusions could be beneficial for patients who are scheduled to undergo low-risk and medium-risk surgeries.

Top up transfusion

a) Low/intermediate risk surgery
   Top-up transfusions where the Hb is less than 90 g/l should be considered for children with no special risk factors who are currently well and having minor (e.g. grommet insertion) or intermediate risk (e.g. umbilical hernia repair) surgery. Aim for Hb 100 g/l post transfusion, and in all cases Hb should not exceed 110 g/l. Consider exchange transfusion in children whose Hb is >90g/l but <100g/l, aiming for a pre-operative Sickle percentage <60. See 'Exchange transfusion', below.

b) Laparoscopic cholecystectomy and laparoscopic splenectomy
In cases where there are no special risk factors, it is reasonable to use top-up transfusions where the Hb is less than 90 g/l. Aim for Hb 100 g/l post transfusion. Consider exchange transfusion in children whose Hb is >90g/l but <100g/l, aiming for a pre-operative sickle percentage <60 in the absence of risk factors, see below. In all cases Hb should not exceed 110 g/l. It is particularly important in this situation to ensure optimal peri-operative and postoperative care, including avoidance of surgery immediately before a weekend. CPAP should be used for 24 hours after surgery, please discuss with PICU consultant in advance.

c) Tonsils/adenoids hypertrophy ± obstructive sleep apnoea
Ensure pre-operative Hb is 100 g/L. This may be achieved by simple top up transfusion in children whose baseline Hb is <90g/l or consider exchange transfusion in children whose Hb is >90g/l but <100g/l, aiming for a pre-operative Sickle percentage <60. In all cases Hb should not exceed 110 g/l. CPAP may be required post-operatively and the likely requirement for this should be discussed with the anaesthetists in advance as it may be necessary to book a PICU bed.

d) Other major abdominal surgery
Either top-up transfusions to Hb 100 g/l (not exceeding 110 g/l) or exchange transfusion (see below; depends on advice of haematologist). Open splenectomy does not need exchange transfusion unless there are other risk factors.

4. Exchange Transfusion

Exchange transfusion is likely to be required if the patient has serious chronic complications e.g. chest crises, stroke or frequent painful crisis, or if their baseline Hb is too high for a simple top up. All elective pre-operative exchange transfusions are undertaken in the Paediatric Haematology Day Unit by automated methods, using the Optia™ apheresis machine. Exchange transfusion should be considered for major surgery, especially when conditions may predispose to sickling. It is mandatory in preparation for:

- major abdominal surgery
- hip/knee replacement
- eye surgery
- organ transplantation
- surgery involving hypothermia or tourniquets (e.g. cardio-thoracic, some orthopaedic)

Exchange transfusion will be organised by the haematologists in the weeks preceding the proposed date of surgery, **which should not therefore be cancelled under any circumstances!**

For patients who need exchange transfusion before surgery as a result of chest crises, frequent painful crises, or major surgery, the HbS level should be < 30%.
For patients with a history of stroke, the aim should be an HbS < 20% in most cases.
For patients undergoing exchange transfusion for low/medium risk surgery whose Hb is >90g/l and <100 g/l, aim for HbS of 60% or lower. Please liaise with the Paediatric Haematology CNS at least 2 weeks in advance of planned surgery so appropriate staffing is in place to undertake automated red cell apheresis in the Day Unit.

5. Procedure for Surgery

Ensure surgeons, anaesthetists, haematologists and nursing staff are aware of the patient and the expected time of surgery.

- Admit the patient to the paediatric ward, not the day care unit, and warn the parents and child that they will need to remain in hospital for at least one night after surgery.
- Start IV fluids when oral fluids are stopped and continue until the patient is able to take oral fluids freely.
- Ensure an oxygen rich environment and monitor SpO_2 for 24 hours after surgery.
- Use 100% oxygen at induction and reversal of anaesthesia.
- Give prophylactic antibiotics (antibiotic choice depends on type of surgery).
- Keep the patient normothermic throughout the perioperative period.
- Use appropriate analgesia and minimise sympathomimetic effects of the pain response.
- Intraoperative transfusion will depend on blood loss and the risk of post-operative complications.

For thoracic surgery and some abdominal and pelvic surgery, including splenectomy, CPAP on HDU or PICU for a minimum of 24 hours after surgery is recommended. Prophylactic post-operative chest physiotherapy, including incentive spirometry, should be instituted. Some children with severe Obstructive Sleep apnoea may need post-operative CPAP on HDU- please discuss each case individually with the Haematology and ENT teams.

6. Pre-operative Sickle Screening in Children

Children from the following ethnic groups should be screened:

African, Afro-Caribbean, Mediterranean (from all around the Mediterranean including North Africa, Greece, Turkey, Cyprus, and Italy) and Middle Eastern.

The important thing from the administrative point of view is that when children are assessed before surgery, a FBC and haemoglobinopathy screen are requested. This will then be done by HPLC, with a sickle solubility test for confirmation only when indicated. The ethnic group should always be stated on the request form.

If sickle cell disease needs to be urgently excluded immediately prior to surgery, patients will need sickle solubility test (urgently) and HPLC (to follow). This will be more costly and will not provide a full diagnosis immediately. It is therefore important that everyone remembers this during the pre-operative assessment and is aware of the ethnic groups who should be tested.

The admitting clinicians (paediatricians or surgeons) will ensure that consent (verbal) is obtained for testing and that an appropriate explanation is given to parents. The paediatric sickle cell CNS will send pink haemoglobinopathy cards and additional information for all children identified as having a haemoglobin trait. All children with newly identified sickle cell disease (SS, SC, SD-Punjab, Sβ thalassaemia) will be referred to the Paediatric Haematology clinic. Sickle cell trait does not require referral.

7. Patients with Sickle Cell trait

These patients are also at risk in situations where there is a risk of hypotension, hypoxia or prolonged application of a tourniquet. They should be well hydrated, oxygenated and kept warm in the peri-operative period as for patients with sickle cell disease. If the need for prolonged tourniquet application is likely, this should be discussed with the paediatric haematologists in advance.

OUTPATIENT MANAGEMENT OF PAEDIATRIC SICKLE PATIENTS

The paediatric haematology clinic is held weekly on Monday afternoons by the lead consultant and lead CNS for Paediatric Haemoglobinopathy. In addition to the consultant and CNS, the sickle cell counsellors, the paediatric dietician, psychologist and social worker are often available.

1. The Aims of the Clinic are to:

- Monitor progress of the children: medical, educational and psychosocial.
- Establish baseline observations for comparison in acute illness.
- Educate parents and children in the management of sickle- related problems.
- Genetic counselling.

2. New Patients

Infants are usually referred following neonatal cord-blood screening. We aim to review them by three months of age. Older patients may be referred after moving into the area or for discussion of more complex problems, eg the role of hydroxycarbamide (hydroxyurea) or consideration of bone marrow transplantation - see Paediatric BMT Guidelines.

- Confirm diagnosis with quantitative Hb HPLC: HbS, A_2, F and other abnormal HbS, e.g. HbC. Check also FBC, retics, U + Es, LFTs and LDH. This should be repeated at 1 year of age when the blood group, red cell phenotype and G6PD level should also be checked.
- Take full personal and family history including names and ages of parents and siblings. Also plans for future children can be discussed.
- Explain to parents the probable diagnosis and its implications, including genetic counselling.
- Weigh, measure height and examine the child.
- Check immunisations.
- Discuss acute complications in infancy including dactylitis, acute splenic sequestration
- Prescribe Penicillin and folic acid if appropriate and give follow-up appointment
- Ensure that a haemoglobinopathy card has been issued, and that the patient and family have contact details for the hospital, the CNS, the consultant's secretary and Accident and Emergency.
- Check that the child is known to the Health visitor, GP and sickle cell counsellor.
- Issue a splenectomy/hyposplenism card.

3. Routine Medication

Folic acid

From	To	Dose
1month	3 years	2.5 mg
3 years	onwards	5 mg od

4. Penicillin V

From	To	Dose
birth	1 years	62.5mg bd
1 year	5 years	125 mg bd
5 years	onwards	250 mg bd

5. Regular Patients

- On arrival, FBC and reticulocytes.
- Weight and height; pulse oximetry; BP if aged ≥10 years. Each patient should have a growth chart.
- Document any sickle-related or other disease since last visit, immunisation up to date, school progress and attendance's and holiday plans. Ask about bed-wetting and symptoms of upper airways obstruction.
- Examination: check especially for jaundice, heart for size and murmurs, liver and spleen size (measure).
- Any questions from parents, involve children as appropriate, any letters to be written.
- Prescribe penicillin (check being taken), folic acid. General Practitioner prescribes anti-malarials if required.
- Initiate (if first visit) or update yellow haemoglobinopathy sheet at the front of the notes
- Make next appointment.**
- Annual review (see appendix 7). All patients should have liver function tests, electrolytes, urea and creatinine, TCD (aged ≥ 3 years).

6. Prophylaxis Against Pneumococcal Infection

There is now very good evidence that penicillin prophylaxis protects against pneumococcal septicaemia / meningitis PROVIDED IT IS TAKEN REGULARLY. It is essential that all children with sickle cell disease take penicillin twice daily continuously, starting by the age of 3 months at the latest. Make sure that the parents are prepared to give it continuously and keep this under review. Pneumovax® (23-valent pneumococcal polysaccharide vaccine) is given to children every 5 years over the age of two, in addition to the 13-valent Pneumococcal Conjugate Vaccine (Prevenar-13®) received as part of the universal immunisation programme. Pneumovax does not give complete protection and is not an alternative to penicillin.

**** Appointments**

Children with Sickle cell disease are seen 3 monthly until 2 years of age and six-monthly thereafter, unless there are medical, educational or psychosocial concerns in which case they should be seen more frequently.

BONE MARROW TRANSPLANT IN SICKLE CELL DISEASE

* Indications for sickle cell disease:

1. Veno-occlusive crisis (VOC) despite hydroxycarbamide: four or more episodes a year requiring hospitalisation or impacting in schooling despite hydroxycarbamide treatment.
2. Recurrence of acute chest syndrome despite hydroxycarbamide.
3. CNS disease:
    a. Stroke
    b. Abnormal Trans-cranial dopplers (TCD) and silent infarct or abnormal psychometric tests/poor school performance formally assessed
    c. Silent infarcts with cognitive deficiency
    d. Significant abnormalities in MRA despite transfusions
    e. Abnormal TCD and generation of red cell alloantibodies
    f. CNS disease requiring transfusions leading to significant iron overload despite best attempt at adequate management

Suboptimal medical care

Disease	**Allogeneic matched related**	**Allogeneic unrelated**	**Haploidentical related**	**Autologous blood or marrow**
Donor specifics	10/10 sibling other 10/10 related 9/10 related	10/10 adult 9-10/10 adult 4-6/6 cord	<9/10 related	
Stem Cell Source	BM/PBPCs/cord	BM/PBPCs/cord	PBPCs/BM	PBPCs/BM
Sickle Cell Disease	Standard of Care	Clinical Option (requires careful assessment)	Clinical Option (requires careful assessment)	N/A

Reference: UK Paediatric BMT Group HSCT Indications, 17 December 2012

6) IMPLEMENTATION

Training required for staff	☑ Yes ☐ No
If yes, who will provide training:	Self-reading
When will training be provided?	At induction
Date for implementation of guideline:	Immediate

7) MONITORING / AUDIT

When will this guideline be audited?	January 2016
Who will be responsible for auditing this guideline?	Kirstin Lund
Are there any other specific recommendations for audit?	No

8) REVIEW

Frequency of review	**Please indicate frequency of review:** Every 2 years **Person and post responsible for the review:** Paediatrics, Pharmacy, Surgery, ENT, PICU

9) REFERENCES

References are included within the main body of the document.

10) GUIDELINE DETAIL

Start Date:	**October 2015**
Approval Dates	**Name of Divisional group:** **Date of ratification:** Children's Quality and Safety Committee Meeting 08/10/15
	Name of Directorate group: **Date of ratification:** Quality Meeting Paediatric Haematology 28/08/15
Has all relevant legislation, national guidance, recommendations, alerts and Trust action plans been considered, and included as appropriate in the development of this guideline?	Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK revised version 2008: UK Thalassaemia Society NHS Sickle Cell and Thalassemia Screening Programme programme, second edition, 2011. BCSH Transfusion guidelines for Children and Neonates, (2004+ Amendments 2005/2007) Blood transfusion guidelines for children and neonates:, ICHT Intranet. Iron chelation guidelines for paediatric patients requiring regular transfusions. ICHT Intranet. Sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital NICE guidelines [CG143] Published date: June 2012 West Midlands Quality Review Service Quality Standards
Have all relevant stakeholders been included in the development of this guideline?	Dr Kirstin Lund: Lead Consultant for Haemoglobinopathy Service Dr Leena Karnik / Dr Josu de la Fuente: Deputy Lead Consultant(s) for Haemoglobinopathy Service Dr Josu De La Fuente: Paediatric Blood and Marrow Transplant Programme Director Dr Leena Karnik: Lead Consultant for Paediatric Haematology Catherine Mkandawire: Haemoglobinopathy Clinical Nurse Specialist/ MDT coordinator Marion Ong: Paediatric Haematology Day Unit Haematology Clinical Nurse Specialist Camilla Barratt Zita Noone: Specialist Social Worker for Haemoglobinopathy Service Becky Armstrong: Specialist Psychologist for Haemoglobinopathy Service
Who will you be notifying of the existence of this guidance?	**Please give names/depts:** Division of paediatrics, including A&E, anaesthetics, and Children's Ambulatory Unit
Related documents	Sickle Cell Pain Management - Paediatric Protocol Transition of haemoglobinopathy patients

	Imperial College Healthcare NHS Trust Paediatric Red Cell Operational Policy
Author/further information	**Name:** Kirsten Lund **Title:** Consultant Paediatric Haematologist **Division:** W&C **Site:** St Mary's Hospital **Telephone/Bleep:** 02032127682 **Trust email address:** Kirstin.Lund@imperial.nhs.uk
Document review history	**Next review due:** October 2017
THIS GUIDELINE REPLACES:	Current Sickle Cell Guideline on the Source

11) INTRANET HOUSEKEEPING

Key words	Exjade, Desferal, PCA, cyclizine, senna, naloxone, chlorpheniramine, hydroxyzine, pain, sickle, girdle syndrome, exchange transfusion, sickle crisis, priapism, phenylephrine, prevenar, pneumovax, hepatitis B vaccine, hydroxycarbamide, Hydroxyurea, spirometry Deferasirox, Deferiprone Paracetamol, Ibuprofen, Diclofenac, Naproxen, Codeine, Tramadol, Morphine, Oramorph, Lactulose, Movicol, Movicol paediatric, laxido, Folic acid, penicillin, Desferrioxamine, meningitis B, dihydrocodeine
Which Division/Directorate category does this belong to?	Women's and Children's
Which specialty should this belong to when appearing on the Source?	Haematology

12) EQUALITY IMPACT OF GUIDELINE

Is this guideline anticipated to have any significant equality-related impact on patients, carers or staff?

Yes ☐ No ☑

Appendix 1. Intravenous opiate infusions

An opiate infusion may be given as long as frequent monitoring of respiratory rate, oxygen saturations and conscious level will be assiduously carried out. A nursing ratio of 1:2 is recommended for all children on intravenous morphine infusions. This is best delivered by Patient or Nurse Controlled Analgesia (PCA/NCA). PCA/NCA must only be set up by staff who have been trained and authorised to programme the infusion pump. See also paediatric PCA/NCA Guidelines.

MORPHINE PCA

Set up values if under 50Kg	
Concentration	20 microgram/kg/mL (wt in kg = amount of morphine in mg; made up to 50mLs with 0.9% saline)
Loading dose	See page10
Bolus (mg)	100 microgram/kg/dose (max 5 mg)
Continuous infusion	10 - 40 microgram/kg/hour = 0.5 - 2.0 mL/hr
Lockout period (minutes)	20 minutes
If respiratory rate falls to <12/min and/or there is a drop in GCS, Stop opiate infusion and inform doctor.	

Links to guidelines:
Paediatric Pain
Morphine PCA / NCA Proforma < 50Kg
Morphine PCA / NCA Proforma > 50Kg

To reverse opiate-induced hypoventilation:

Naloxone should always be prescribed

From	To	Dose
1 month	18 years	IV - 4 micrograms/kg, subsequent dose of 100 micrograms/kg if no response.

Use of an airway and O_2 mask may be required.

Note on withdrawal from opiates

It is advised that patients who have required a PCA/infusion should remain in hospital for at least 24 hours after discontinuation of the PCA/infusion to ensure that he/she does not suffer from recurrent pain or opiate withdrawal.

Appendix 2. Vaccination Schedule

1. Routine childhood vaccinations

Routine childhood vaccinations are recommended for all children with sickle cell disease. Prevenar® is now part of the routine vaccination programme.

Please check Government Guidelines as changes do occur. DoH GreenBook

Additionally, children with Sickle Cell Disease should receive vaccination with Pneumovax every 5 years from age 2, annual live influenza vaccine from age 6 months

2. Hepatitis B Vaccine

Recommended for all children with HbSS and HbSb^{o}thalassemia, mandatory for children receiving blood transfusions)

Injection	Dose
1st	0.5 mL IM
2nd, 1 month after the first dose	0.5 mL IM
3rd, 6 months after the first dose	0.5 mL IM

All children requiring blood transfusions, whether as an elective or emergency procedure should receive Hepatitis B vaccination. Hepatitis B antibody levels should be checked 2 - 4 months after 3rd dose to ensure an adequate response (>100 iu/mL). Thereafter, antibody levels should be checked every 5 years and a booster given if levels are sub-optimal.

Influenza Vaccine is recommended for all patients each autumn. The live vaccine should be avoided in patients on Hydroxycarbamide/steroids or with other known immunodeficiency. In these context the inactivated influenza vaccine is recommended.

BCG is recommended, preferably at birth. If this is not administered at birth, follow the RCPCH guidelines.

3. Additional vaccines for splenectomised children:

Box 7.1 of the Green Book should be referred to for splenectomised children:

Link to Green Book chapter 7

4. Malaria Prophylaxis

- Depends on area to be visited. Consult with GP or Hospital for Tropical diseases
- Check G6PD status
- To be commenced 1 week prior to departure and to be continued throughout visit and until 4 weeks after return. Patients going to live in malarial areas should be advised to stay on prophylaxis lifelong if possible.
- General advice re preventing bites – mosquito nets, clothing, repellents should be given.

Appendix 3. Hydroxycarbamide

Hydroxycarbamide reduces the frequency of painful crisis, chest syndrome and transfusion requirements in both adults and children with severe sickle cell disease. It also appears to improve growth and possibly prevent hyposplenism in children. It has not been proven to prevent stroke or avascular necrosis in joints, and currently it is the subject of ongoing trials in Europe and North America. Caution is advised, however as its long-term profile in terms of toxicity, mutagenicity, teratogenicity and leukaemogenic potential is unknown. Careful discussion of these issues with the parents prior to commencing hydroxyurea is essential, and parental consent should be recorded in the patient's notes. **The decision to start hydroxycarbamide must only be made after discussion with a Paediatric Haematology Consultant.**

Patient Exclusion criteria

- Age < 2 years
- Regular transfusion regime
- Abnormal liver function tests (AST or ALT > x2 upper limit of normal)
- Inability to attend clinic regularly for follow-up

Patient Eligibility

Patients (HbSS or Sb-thalassaemia, *not* HbSC) with a severe clinical course *may be offered* hydroxycarbamide i.e. with

either: 3 admissions with painful crisis within one year
or Frequent days of pain at home, leading to a lot of time off school
or Recurrent acute chest syndrome

The following predict a more severe clinical course and are additional reasons *to consider offering* hydroxycarbamide if a child also has severe clinical symptoms:

Steady state values:	Hb <70 g/l WBC >15 x10^9/l HbF <6%
Renal insufficiency due to sickle cell disease	

Dose & Monitoring

- Start at 15 mg/kg/day (if old enough to swallow capsules then round up to the nearest 500mg/day). If no or poor response increase dose by increments of 5 mg/kg/day every 8-12 weeks (max: 35 mg/kg/day)
- Monitor FBC, HbF level and retics, every 2 weeks initially, then 4 - 8 weekly when on a stable dose
- Monitor biochemistry profile (hydroxycarbamide has renal excretion & hepatic toxicity)
- Assess clinical response after 9 - 12 months. If being treated for painful crises, if there is no improvement at this time, consider stopping - discuss with Consultant.
- Stop treatment if any of the following occur:
    - Neutrophils < 1.5 x10^9/l
    - Platelets < 80 x10^9/l
    - Retics < 80 x10^9/l
    - Hb < 55 g/l
    - Hb drops by more than 20% from baseline, or > 20 g/l
- If treatment is interrupted, check FBC weekly and restart after counts recover, at a dose lower than the patient was on at the time toxicity developed
- Aim to give the maximum tolerated dose (MTD), but if haematological and clinical responses are achieved at a lower dose consider using this dose.
- Hydroxycarbamide may need to be stopped during an acute admission when sepsis is known or suspected.

Appendix 4. Transfusion Record

St MARY'S HOSPITAL

TRANSFUSION RECORD

Name : **Hospital Number :**

Type of SCD:
On iron chelation: (tick as appropriate) **DFX** ☐ **DFP** ☐ **DFO** ☐ **Combination** ☐
Indication : **Start Date :**
Aims :

DATE	PRE TX Hb	PRE TX S%	POST TX HB	POST TX S%	VOLUME OF BLOOD	FERRITIN	ALT	Creatinine	NOTES

Ophthalmology review : **Audiology review :**

Hepatitis BsAg: **Hepatitis C Ab :**

Appendix 5. Exchange Transfusion

A total exchange is 1.5 - 2 times the child's blood volume. This is normally performed in 3 - 4 exchange procedures.

Each exchange procedure should be calculated at 30 mL/kg

A child of 25 kg x 30= 750 mLs

Childs Hb 70 g/l thus start with saline 10 mL/kg =
250 mL saline in and 250 mL blood out
Then 20 mL per kg of blood = 500 mL blood in and 500 mL out

N.B. If starting Hb below 60 g/l all blood should be used = 750 mL blood in and 750 mL blood out. Record in 10 - 15minute cycles.

For example:

Time	Saline in	Blood in	Blood out	Balance
10.00-10.10	31		31	31 in 31 out
10.10-10.20	31		31	62 in 62 out
10.20-10.30	31		31	93 in 93 out
10.30-10.40	31		31	123 in 123 out
10.40-10.50	31		31	154 in 154 out
10.50-11.00	31		31	185 in 185 out

This example is typical of that required for a clinically unstable patient; slighter higher rates may be used in patients who are cardiovascularly and neurologically stable (see main text for further information on volumes and overall timing).

Appendix 6. References for growth management

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Appendix 7a. The Annual Review

The Annual Review should include the following:

- Assessment of progress in general and a review of the patient's and family's knowledge of the condition.
- Review of information provided – to include any investigations taken, treatment given etc
- Clinical measurements – undertaken at visit or results of investigations since last visit reviewed
    - Clinical examination – heart, lungs, liver, spleen
    - Weight and height (plotted on centile charts)
    - Assessment of puberty
    - Blood pressure
    - Oxygen saturations (on air)
    - Urinalysis
- Clinical review
    - Number of hospital admissions
    - Number and severity of crises (include days off school)
    - Other complications eg splenic sequestration, aplastic crisis, priapism, gallstones, chest syndrome, stroke
    - Nocturnal enuresis >6 years
    - Assessment of child development
- Review of infection prevention
    - Penicillin V dosage and compliance
    - Immunisation record
- Consideration of other treatments eg hydroxycarbamide, bone marrow transplantation.

Appendix 7b.

ST MARY'S PAEDIATRIC HAEMOGLOBINOPATHY CLINIC:
Sickle Cell Disease Annual Review Checklist: investigations and management

Date of review:……

Name
Hospital Number

Diagnosis:……

Other co-morbidities or diagnoses:

1………

2……

3......

4……..

Consent for NHR given: Yes/No

Shared care centre (if applicable): …….

Observations:

Height (cm)…… ...Centile…….....Weight (kg) .....Centiles…….....

BP(mm of Hg)……..... Oxygen Saturation…… Urinalysis:.....

Hospital Admissions in last 12 months:

Number of hospital admissions:……..

Number of admissions for pain crises……

Other acute complications in last 12 mths?: (tick as appropriate)

Stroke ☐ Dactylitis ☐ Chest syndrome ☐ Aplastic crisis ☐

Febrile episode requiring admission ☐ Osteomyelitis ☐

Splenic sequestration ☐ Hepatic sequestration ☐ Priapism ☐

Other (specify)……

PICU needed Yes/No
Number of PICU admissions……..

Chronic complications: (tick as appropriate)

Pubertal delay ☐ Poor growth ☐

Surgery in the last 12 months: …….

Medications:

Penicillin Yes/No Dose……. Compliance: …….

Folic Acid Yes/No Dose……. Compliance: …….

Hydroxycarbamide Dose……..Compliance: …….

Name Hospital Number

Other medication (if any)

1. …… Compliance:……

2. …… Compliance: ……..

3. …… Compliance:…….

4. …… Compliance: ……

Immunisations:

Pneumovax date given……Hepatitis B date given……

Annual flu jab in last 12 months:

Symptoms review:

Painful crises: Yes/No.

Average number of crises per month/school term**:** ……..

Enuresis (if child is >6y): Yes/No. Number of nights/wk……..

Snoring: Yes/No **Daytime somnolence**: Yes/No

Chronic pain: Yes/No **Location**……..

Shortness of breath on exertion Yes/No

Stuttering priapism Yes/No Maximum duration:……. Frequency…….

Menarche achieved: Yes/No

Schooling and education:

Name of school……. Academic year……

Attendance (Percentage in last school term)…….

School performance: Satisfactory/Unsatisfactory

Memory and concentration: Good/Poor

Statement of special education needs in place: Yes/No

Examination:

Hepatomegaly: Yes/No Size(cm)…..... Splenomegaly Yes/No Size(cm)…....

CVS……Respiratory…….

Tonsils……Lymph nodes ……

Other (specify)…….

……

Name

Hospital Number

Annual investigations: Date……

TCD (TAMMa) RMCA cm/sec……LMCA cm/sec ……

Children not on regular transfusions:

Baseline Hb(g/dl)

Reticulocyte count($x10^9$/l)……. Bilirubin (μmol/l)……..

Creatinine (μmol/l)…….. Vitamin D(nmol/l)……..

Hepatitis B serology: Anti HBs antibody (miu/l)……Protective/Not protective

HBsAg/antiHBc…… HepC Antibody……..

Management changes considered:

Hydroxycarbamide Yes/No/Not applicable

BMT referral Yes/No/Not applicable

Transfusion programme Yes/No/Not applicable

Psychologist Yes/No/Not applicable

? Dietician

Refer to other clinics Yes/No/Not applicable (specify if yes)…….

Other (specify)……

Name of person completing annual review……

Appendix 8. Incentive Spirometry Guidelines in children with Sickle Cell disease.

Patient Selection

All patients of 6 years and older with sickle cell disease who fulfil one or more of the following criteria:

- Acute chest, back or abdominal pain
- Receiving opiate analgesia and prolonged immobility e.g. post fracture, limb pain
- Pre-op and post-op abdominal surgery
- Consultant or Clinical nurse specialist specifically requests

Initiation of Incentive Spirometry Programme

The doctor on the ward or specialist nurse should: -

- Select the patient for the incentive spirometry programme
- Document selection in the medical notes
- Inform the nurse in charge of that shift
- Refer all participants to the physiotherapist in order that the physio may monitor their chest and teach the family how to use the device

The nurse in charge of the shift has responsibility for ensuring that the programme is commenced and that the appropriate documentation is completed.

Documentation

- Incentive Spirometry record sheets and the care plan will be kept in the patient's bedside charts folder
- The record sheets will be filed in the patient's medical notes
- A list of participants in the programme will be kept by the physiotherapists and the clinical nurse specialist (Haemoglobinopathies)

Incentive Spirometry Programme

- 10 maximal inspirations for a 3 second hold using the incentive spirometer every 2 hours from 08.00 to 22.00 and while awake at night
- Documentation will include measurement of pain scale and SaO_2 prior to incentive spirometry and recording of maximum inspiratory capacity achieved following incentive spirometry
- Incentive spirometry to be carried out with the patient sitting in an upright position
- Patients requiring > 35% oxygen should continue oxygen therapy via nasal specs during breaths or via oxygen tubing attached to device

Discontinuation of Programme

Medical staff or physiotherapist will be responsible for deciding when to discontinue the incentive spirometry programme. Patients should fulfil all of the following:

- Chest, abdominal and/or back pain subsided
- Opiate analgesia discontinued/ mobilising independently
- No clinical signs of a respiratory infection

OR

- Medical staff consider patient unfit to continue for medical reasons

[Paediatric Physiotherapy]

Appendix 9. Incentive Spirometry Care Plan

Patient Name:	Hospital Number	Admission Date:	Ward:	DOB:	Weight (Kg):

Date/ Time	**INCENTIVE SPIROMETRY CARE PLAN** *For patient with Sickle Cell Disease identified for use of Incentive Spirometry Guidelines by Doctor or Clinical Nurse Specialist to reduce risk of respiratory complications*	**Date Reviewed/ Discontinued**	**Name in BLOCK CAPITALS & Signature of Registered nurse**
	Please indicate **reason for selection** of patient for Incentive Spirometry: • Acute chest, back or abdominal pain • Receiving opiate analgesia and prolonged immobility e.g. post fracture, limb pain • Pre-op and post-op abdominal surgery • Consultant or Clinical nurse specialist specifically requests		
	Analgesia given:		
	Analgesia Route: (please circle) ORAL / I.V.		
	Incentive Spirometry Volume Goal in mL: (minimum 20mL/Kg)		
	When Incentive Spirometry has been stopped, please indicate **reason for discontinuation**: • Chest, abdominal and/or back pain subsided • Opiate analgesia discontinued/ mobilising independently • No clinical signs of a respiratory infection • Medical staff consider patient unfit to continue for medical reasons		
	Did the patient develop signs of respiratory complication during hospital admission, i.e. new infiltrate or collapse on chest X-ray or respiratory symptoms? (please circle) YES/ NO **If yes, please specify**:		
	• **Position** - patient should be in an upright position whilst using the Incentive Spirometer • **Oxygen Requirement** – If the patient has supplementary oxygen prescribed, continue this via nasal specs during breaths • **Frequency** - The patient should be encouraged to take 10 maximal inspirations using the Incentive Spirometer with a 3 second hold every two hours between 08.00hrs and 22.00hrs • Patient should be referred to the physiotherapists, in order that they are aware of their condition and can monitor his/ her chest • Record on **Incentive Spirometry Record Sheet** throughout use with patient		

[Paediatric Physiotherapy]

Appendix 10. Incentive Spirometry Record Sheet

Patient Name:	Hospital Number:	Male/Female:	D.O.B:

INCENTIVE SPIROMETRY RECORD SHEET

Date & Time	Pain Score (0-10)	Oxygen Requirement (%)	Oxygen Sats	Respiratory Rate	Incentive Spirometry Done?		Maximum Inspiratory Capacity (mL)
					Yes	No	

[Paediatric Physiotherapy]

Appendix 11. Exchange Transfusion Form

Time	Saline in	Blood in	Blood out	Balance

Appendix 12. Preparation of Child with Sickle Cell Disease for Surgery

To be completed prior to surgery using peri-operative guidelines

Patient Name Dob: MRN: Ward: Consultant Surgeon: Consultant Haematologist: Planned Procedure:	FIX PATIENT LABEL HERE

Documentation			
			Initial & date
Procedure booked			
Special instructions:			
Consent Complete			
Have Anaesthetists been informed			
PICU / HDU booked? CPAP?			
	Yes	**No**	**Not applicable**
PRE-OP BLOODS			
Red Cell Phenotype (if not known), Group and save, FBC, Biochemistry with CRP, Clotting Screen with Fibrinogen, S%			
Ensure Cross match done within 72 hours of surgery			
Bloods checked and results satisfactory and documented			
Blood ordered for 07.30am on day of procedure			
X ray/ scans/ ECG/Sleep study			
PRE-OP TRANSFUSION			
Haemoglobin Platelets			
PT APTT			
Fibrinogen			
S%			
Surgery			
	Yes	**No**	**Not applicable**
IV fluids from nil by mouth until drinking freely			
Oxygen rich environment until fully awake. Monitor oxygen saturations for 24 hours post-surgery			
Prophylactic antibiotics			
Pain management Plan			
Discuss pain management			