1. Introduction and Who Guideline applies to

This guideline outlines the management of patients with sickle cell disease who are admitted acutely to hospital. Sickle cell disease (either HbSS or compound heterozygous states including HbSC and HbS/B-thalassaemia) affects up to 15000 patients in the UK. The commonest reason for admission to hospital is acute pain, which can occur in any part of the body but most often affects the limbs. Sickle pain is usually very severe and often requires opiate analgesia. Patients often have analgesia at home which they take before coming into hospital and can often verbalise if this is their 'usual' sickle pain.

The pathogenesis of sickle cell pain is thought to be due to deoxygenated sickle haemoglobin forming large polymers which cause red cells to become deformed and obstruct small blood vessels. Triggering factors include cold weather, dehydration, exam stress, pregnancy but often no cause is found.

These guidelines may be used by medical and nursing staff in any area of the hospital. Any admission of a patient with Sickle Cell Disease should be discussed with the Haematology team on call. They outline the care of patients admitted with acute complications of sickle cell disease.

2. Guideline Standards and Procedures

This guideline outlines the management of patients with sickle cell disease presenting with acute complications. As described, the commonest reason for admission is acute pain but other, potentially life threatening complications are also discussed.

- The local policy for this trust is shown in Appendix 1.
- A summary of this guideline document is available in Appendix 2

Arrangement for admission

- All patients known to the local haemoglobinopathy team will have been made aware of how to contact the clinical teams for advice, including out of hours. Each hospital will have their own system for ensuring open access for urgent medical review

Immediate assessment

- Baseline observations must be performed as standard and NEWS documented. Escalations should be carried out in line with Local policy. If opiates have been administered by the ambulance crew, this MUST be documented clearly.
- Baseline oxygen saturations must be documented ON AIR. If <95%, ABG should be performed and more urgent escalation to haematology considered.
- Suspected sepsis should be managed in line with local policy

1. Acute Painful episode

1.1 Pain management

- A pain score MUST be documented. Analgesia should be addressed as a priority and in line with NICE quality standards, **analgesia must be administered within 30 minutes of admission (NICE CG143).**
- IV access is NOT mandated in all patients and delays for attempted cannulation is not an acceptable reason for not meeting this target.
- Entonox may be required until the first dose of analgesia is administered but must not be continued after opiate analgesia has been given.
- As part of the annual review process, individualised care plans may be available on local hospital systems. If unavailable, patients should be managed as per the local painful crisis flowchart (See Appendix 1).
    - Some complex patients with frequent ED attendance may also have a individualised care plan available. Please refer to local procedure.
- If the pain is their 'usual sickle pain', patients will often have taken their own analgesia at home. This should be taken into consideration when prescribing analgesia. Opiate analgesia is most often required, providing baseline observations are stable.
- Opiate naïve patients should be assessed based on their pain score and analgesia offered in line with the WHO analgesic ladder (below):

Step 1: mild pain
Non-opioid ± adjuvant: Paracetamol 500mg-1000mg + Ibuprofen 400mg TDS
Step 2: moderate pain
Weak opioid (or low dose of strong opioid) ± non-opioid ± adjuvant: As above for mild pain + Dihydrocodeine 30-60mg (maximum dose 180mg daily)
Step 3: severe pain
Strong opioid ± non-opioid ± adjuvant As above for moderate pain + Morphine sulphate (see text)

- Morphine should be given via the most appropriate route. Some patients recently transitioned from paediatric care may prefer oral morphine and this should be offered. Unless otherwise documented, subcutaneous morphine should be given. Intravenous morphine is not recommended as routine.

- **<u>If the patient does not have a dedicated analgesia plan, then give based on weight:</u>**
    - If ≤50kg, give 5mg morphine sulphate SC stat
    - If >50kg, give 10mg morphine sulphate SC stat

Efficacy of analgesia should be assessed after **30 minutes** and a further dose or weight appropriate SC morphine administered provided that there is no evidence of opioid toxicity.

- If the RR is <10 per minute, omit opioid analgesia
- If RR <6, give naloxone 100microgram every 2 minutes as necessary

Pain should then be reassessed every 30 minutes until adequate pain control achieved.

If pain control is inadequate despite 2 doses of morphine:

- Discuss the case with the on call haematology registrar (mobile via switchboard) or local haemoglobinopathy nursing team (during working hours) and review patient specific care plan (if available)
- Consideration of escalation to patient controlled analgesia (see protocol)
- Consideration of alternative causes of pain if out of context with 'usual' sickle pain.
- Once pain is controlled, regular adjunct analgesia and PRN opiate analgesia (0.05-0.1mcg/kg to nearest mg every 2 hours) should be prescribed.

Adjunct analgesia	
Paracetamol 1gram IV/PO	Up to 4 gram in 24 hours
Ibuprofen 400mg PO	Up to maximum dose of TDS unless contraindicated (such as patients with known renal issues)
Dihydrocodeine 30-60mg PO	Up to maximum dose of 180mg daily
Lidocaine 5% topical patches	Offer to all patients unless contraindicated
Non-pharmacological methods: Local heat packs TENS machine	 May be available from haemoglobinopathy team If available

Alternative analgesics such as oxycodone, ketamine, methadone and fentanyl should only be used after discussion with the acute pain team and consultant haematologist unless specifically indicated in the patients care plan documentation.

Requirements for analgesia should be reconsidered on a daily basis by a haemoglobinopathy specialist team.

1.2 Adjunct medication

Antipruritics:

- Prescribe PRN chlorphenamine 4mg PO or hydroxyzine 25mg BD max

Antiemetics:

- First line: Ondansetron 4mg BD IV/PO
- IV cyclizine use should be avoided

Laxatives:

- Ensure regular laxatives are prescribed if on regular morphine. Patient's choice should be taken into consideration.

Stomach protection:

- Give concurrent PPI (Lansoprazole 30mg) if on NSAIDs

Folic acid:

- Patients will be on regular folic acid 5mg OD long term, ensure this is prescribed on regular chart.

Oxygen:

- There is no evidence for this being used routinely in call cases of painful crisis
- Its use should be dictated by the clinical situation and oxygen saturations
    - If sats <95% on air, perform ABG and give supplementary oxygen (titrated to maintain sats >98%)
    - If increasing oxygen is required, urgent medical review is required to assess for acute chest syndrome

1.3 Baseline Investigations

- Blood tests: FBC, Reticulocytes, Biochemistry (U&Es, LFTs, LDH, CRP), G&S
- Reasonable attempts should be made to perform baseline investigations in admission area. If unsuccessful due to difficult venous access this should be deferred until the patient is admitted to haematology **unless more urgent results are clinically indicated.**
- Haemoglobin electrophoresis only indicated if a new patient or patient recently transfused
    - If recently transfused (within 12 weeks), also request DAT/G&S (via blood bank)
- If appropriate: Blood cultures, Urine dipstick +/- MSU, Throat swabs (if viral symptoms), viral serology, COVID swab
- CXR **not** routinely required: perform if dyspnoea, O2 sats<95%, increased respiratory rate, cough, fever or chest pain

1.4 Other considerations

Hydration:

- Patients requiring admission for a sickle crisis and who cannot take oral fluids need proper hydration evaluation and careful management.
- Assess hydration status: calculate according to degree of dehydration plus maintenance fluids
- Not all patients require IV fluids but all patients should be on a fluid balance chart and supplementary fluids given if necessary

Antibiotics:

- Most patients will be on long term prophylaxis with penicillin 250mg BD. If admitted and therapeutic antibiotics are not required, this should continue
- If the patient is febrile or has a history suggestive of an infective cause of the sickle cell crisis they should be commenced on antibiotics in line with the Local microbiology guidance

Thromboprophylaxis:

- Sickle cell disorders are associated with an increased risk of thrombotic complications
- All patients should be VTE assessed on admission and offered LMWH prophylaxis, unless contraindicated
- Anti-embolic stockings should **not** be used

Transfusion:

- See local transfusion guidelines
- Any transfusion in sickle cell patients, other than for life threatening haemorrhage, should be discussed with the local haematology team.

Ongoing patient monitoring:

- Observations should be carried out every half hour until pain is controlled.
- Respiratory rate and O2 saturation should be checked 1-2 hourly while on opiate analgesia. GCS and pupil size should also be noted.
- Temperature, BP and pulse, and fluid balance should be reviewed 4 hourly.

2. Other acute presentations

2.1 Acute Chest Syndrome (ACS)

This is a life threatening complication of sickle cell disease and can arise during a painful crisis or occur on admission.

Clinical Features - some, but not all, of the following may be present:

Chest Pain	Hypoxia (sats <95% or >3% below baseline)	Wheeze
Cough	Tachypnoea	Fever
Shortness of breath	Tachycardia	Fall in Haemoglobin

Differential Diagnosis:
Acute Infection (including COVID-19 infection)
Pulmonary Embolism
Opiate Toxicity
Fluid overload
Hypoventilation due to pain
Asthma exacerbation

Diagnosis and Investigations

Based on:

- Clinical suspicion (low sats, hypoxia on ABG, new chest signs)
- CXR: new pulmonary infiltrate
- Perform baseline investigations (as above)
- Microbiology: blood and sputum culture, atypical serology, flu swabs (if applicable)

Management

- Preventative measures:
    - Vigilance
    - Incentive spirometry for all patient if chest/rib pain on admission (and use as adjunct to treatment)
    - Early treatment of pain and infection with careful monitoring for opioid toxicity
    - Careful hydration management to avoid fluid overload
- Intervention if ACS suspected:
    - Inform haematology registrar/consultant (if not already aware)
    - Early liaison with HDU/outreach team as transfer may be necessary
    - Start appropriate antibiotics to include atypical cover
    - Chest physiotherapy
    - Nebulised bronchodilators may be useful
- Role of transfusion:
    - Simple top up may be adequate, especially if Hb decreased from baseline;
    - Manual or automated exchange transfusion preferable in deteriorating patient or risk of hyperviscosity due to baseline Hb (see transfusion guidelines)

2.2 Acute Anaemia

- Presentation with pallor or extreme lethargy
- Investigations: FBC and reticulocytes, parvovirus serology, urgent cross match
- Consider underlying pathology including parvovirus infection, sequestration, folate deficiency or acute oxidative haemolysis if known G6PD deficiency. Screen for DHTR/Hyperhaemolysis if recent transfusion.
- Check parvovirus PCR if serology negative and high clinical suspicion.

2.3 Acute Stroke

- May be ischaemic or haemorrhagic
- Patients should be assessed and initially managed in line with the local acute stroke guideline with urgent CT head
- Thrombolysis should be considered in sickle cell patients with acute cerebral thrombosis who otherwise meet current UK national recommendations, but these cases should be discussed with a senior haematologist and stroke physician
- Urgent exchange transfusion should also be performed to reduce HbS% to <30%. Acutely, this may need to be performed as a manual exchange with an automated exchange at the earliest opportunity.
- Following acute intervention, an MRI/A head should be performed to assess for sickle related vasculopathy and determine long term management
- Other causes of stroke seen in adults without sickle cell disease should also be considered

2.3 Acute Sequestration

- Sudden enlargement of the spleen (or more rarely, liver) in which blood is pooled in the organ leading to a severe reduction in circulating red cells and profound anaemia
- Abdominal examination will reveal an enlarged spleen or liver
- Urgent FBC and retics followed by urgent cross match as a top up transfusion. See 'Transfusion in sickle cell disease guideline' for more information.

2.4 Abdominal Pain

Patients can present with abdominal pain for a number of reasons. The differential diagnosis includes (not exhaustive list):

Gallstones	Referred pain	Acute splenic/hepatic sequestration
Pancreatitis	Appendicitis or other infection	Constipation
Bowel Ischaemia	Thrombosis i.e. renal vein	Vaso-occlusion

Investigations:

- FBC, retics, U&Es, LFTs, Coag, Amylase, Blood cultures, MSU
- Relevant imaging, as guided by clinical features/findings
    - Take radiation exposure for patients with frequent admissions into consideration

2.5 Priapism

Defined as a prolonged penile erection which is maintained without sexual stimulation and persists despite ejaculation and orgasm.

There are two types:

Stuttering (recurrent episodes lasting <30mins)

Ischaemic fulminant (>3 hours) – should be treated as a medical emergency.

Management

- Hydration, analgesia, encourage micturition
- Etilefrine 50mg may be given by mouth (available from main pharmacy)
- Urgent referral to on call urology registrar
- If persists > 3-4 hours, then aspiration of corpora cavernosa (with or without irrigation) may be required with the instillation of adrenergic agonist e.g phenylephrine, progressing to a surgical shunt procedure if not successful
- Transfusion therapy is not thought to be useful in acute presentation although it may be considered if all other treatment is ineffective

2.6 Sepsis – including osteomyelitis

- Patients with sickle cell disease are immunocompromised and any features of infection should be managed in line with the local sepsis policy
- Osteomyelitis should be considered in any patients with a hot and painful limb
- XR should be performed, but may be normal and MRI is likely to be required
- Blood cultures should be sent in any febrile patient
- Microbiology advice should be sought for suspected cases to ensure adequate pathogen cover in line with local policy

2.7 Renal complications

- Patients with sickle disease are at increased risk of nephropathy and renal impairment. U&Es should be performed as part of baseline investigations for all patients presenting to hospital.
- Haematuria may occur and can be associated with papillary necrosis. This may be associated with ureteric colic and can lead to significant blood loss. Treatment is supportive and urological support may be required for renal irrigation.
- Other causes of renal impairment and haematuria should also be considered.

2.8 Visual loss

- Sickle cell disease is associated with retinopathy and any visual loss should be considered a medical emergency
- Patients should be advised to attend local eye casualty at their local hospital for urgent review.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
NICE pain score audit data	Regularly submitted to NHS England haemoglobinopathy dashboard and reviewed at East Midlands haemoglobinopathy network	Amy Webster	Quarterly	Via dashboard

5. Supporting References (maximum of 3)

Sickle cell society Standards for the clinical care of adults with sickle cell disease in the UK, February 2018

6. Key Words

Sickle cell disease, painful crisis, acute complications

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Dr Amy Webster, Consultant Haematologist	**Executive Lead**
Details of Changes made during review: Formatting changes Update to appendix to display local relevant procedures	

Appendix 1:

UHL Policy for admission and management of adult patients with sickle cell disease

Adult patients with sickle cell disease have direct access to **Osborne Assessment Unit** (0116 258 6681). Admissions may be advised after contact with the clinical nurse specialist or out of hours call to the haematology emergency phone number (08081782212).

Patients may self-present to ED or rarely be diverted if OAU cannot directly accept the patient.

Any patient admitted should be discussed with the on call haematology registrar or consultant, if unavailable.

Sickle cell disease is a multi-system disorder and referral to non- haematology specialists may be advised but the haematology team will remain involved.

If there is any delay in transfer from ED to a haematology ward, the haematology registrar will arrange for the patient to be seen and assessed in ED.

Once admitted under haematology, they will be under the care of the red team.

ALL patients should be assessed and monitored in line with this policy

Advice from the haematology team can be sought via any of the following:

Haemoglobinopathy nurse specialist (Tues-Fri) 07950891490

Haemoglobinopathy Team office (Mon-Fri) 0116 258 6081 (Extension 16081)

Haematology registrar (24/7) – Available via switchboard

Acute painful crisis management – Summary

As per NICE guidance, all patients should be offered appropriate analgesia within 30 minutes. This will be prospectively audited and reported to the team on a quarterly basis

SC morphine is first line and should be given as preference. Some individualised care plans may have alternative management – these are available on OAU for all patients known to the service or ED shared drive for frequent attenders.

Patients new to area should be managed initially in line with local policy. Contact should be made with their parent team at the earliest opportunity for individualised information.

Any patient on opioid analgesia should be monitored in line with the local policy.

Any clinical concern should be escalated to the on call haematology team (out of hours) or the haemoglobinopathy team (9-5, Monday to Friday)

University Hospitals of Leicester NHS
NHS Trust

UHL management of adults patients
with acute complications of sickle cell disease

Flow Chart for management of acute sickle cell admission with painful crisis

Assessment of EWS, including oxygen sats on air and documentation of pain score.

Administer analgesia in line with WHO analgesic ladder (Box A), within **30 minutes** of arrival

Re-assess after 20 minutes

Is pain adequately controlled?

N

Y

Box A: Management of pain: See patients individualised care plan (if available).

Mild pain: Offer paracetamol (0.5-1g) +/- dihydrocodeine 30-60mg +/- ibuprofen 200-400mg

Moderate/severe pain: Morphine sulphate SC (weight based dose).

If ≤50kg = 5mg; If >50kg = 10mg

BOX B: General measures

For ALL patients:

Keep warm and well hydrated.

Avoid IV cannulation unless clinical need

Assess fluid status and commence fluid balance

Assess for sepsis and treat with antibiotics if indicated

Document patients weight

Assess for opiate toxicity

RR<12, new oxygen requirement or sats <95%, drowsy or pin point pupils

If none of the above are present, administer a 2nd dose of SC morphine sulphate

Re-assess after 20 minutes

Is pain adequately controlled?

Y

N

Full patient assessment

History and clinical examination (to include potential triggers, infective signs/symptoms, history of sickle cell complications, transfusion history)

Continue general measures (Box B)

Complete routine investigations (Box C)

VTE risk assessment: Offer LMWH unless contra-indicated

BOX C: Routine Investigations

Bloods: FBC, U&E, reticulocytes, LFT, CRP, G&S

+/- cultures (if indicated)

Urine dipstick
+/- MC&S (if indicated)
+/- Pregnancy test (if indicated)

Imaging: CXR if dyspnoea, Sp02 <95%, fever, cough, chest pain

Are there any features of a red flag event? See Box D

Y

N

Escalate to Haematology team:

- *Consult local policy for advice on contacting haematology in the trust.*
- If outside these hours or patient clinically unwell, call on-call haematology registrar via switchboard

BOX D: Red flag events (see overleaf for further details)

- Acute Chest Syndrome
- Aplastic Crisis
- Stroke
- Priapism
- Acute Abdomen
- Splenic Sequestration
- Suspected delayed haemolytic transfusion reaction

Ongoing assessment

Monitor observations every 30 minutes if morphine administered

If unable to tolerate oral fluids, start IV fluids at 10-20mls/kg

Ensure regular analgesia prescribed

Review results of investigations

Admission to haematology

Once stable and pain controlled, discuss with haematology registrar to arrange admission to Osborne Assessment Unit

If no morphine required, EWS 0 and investigations reviewed, could consider A&E discharge. Discuss with haematology team prior to discharge

Not for blood transfusion unless discussed with haematology

Acute Chest Syndrome

- Life threatening complication; Defined by fever and/or respiratory symptoms in presence of new infiltrates on CXR. New hypoxia should trigger investigation (sats <95% air or >3% decline from baseline)
- Infective cause common and antibiotic therapy (including atypical cover) should be initiated
- Perform ABG if sats <95% **on air** or >3% decline from baseline; Discuss all hypoxic patients with the on call haematology registrar. Ensure routine investigations completed.
- Transfusion should be considered early (top up or exchange) and refer early for HDU/ITU input

Stroke

- Assess initially in line with UHL stroke and TIA guideline.
- Inform haematology team on arrival.
- Emergency management of stroke in SCD patients includes:
    - Need for urgent exchange blood transfusion. Ensure G&S has been sent as part of routine investigations to allow for efficient blood ordering.
    - Consideration of thrombolysis in patients who otherwise fulfil local criteria. All cases should be discussed with the haematologist on call.

Priapism

- Defined as fulminant if > 3 hours duration
- Offer analgesia in line with acute painful crisis protocol; Ensure hydration and encourage micturition
- Inform haematology and urology teams on patients arrival
- Give etilefrine 50mg PO stat (unless contraindicated)
- Consider aspiration of corpora cavernosa if persistent
- Admit under urology team with haematology input

Suspected Delayed Haemolytic transfusion reaction

- Sickle cell patients are at increased risk following transfusion
- Any patient presenting within 7-14 days after a transfusion with signs of a crisis should be investigated for evidence of DHTR.
    - May also present with symptoms of anaemia, jaundice +/- ‘coca-cola’ coloured urine
- In addition to routine investigations, request a Direct Antiglobulin Test (DAT) via blood bank
- Manage crisis in line with acute painful crisis protocol

Acute Vision Loss

- Sickle cell patients are at increased risk of retinopathy
- Any patient experiencing symptoms of vision loss should be seen and assessed in Eye Casualty (or ED if not available)

Appendix 2: Guideline Summary (Quick Reference Guide)

Acute Presentation	Best Practice	Where can further guidance be found?
Pain	Rapid assessment (basic observations, pain score): Appropriate pain relief within **30 minutes** – in line with policy or patients care plan Monitor every 30 mins till pain relieved then 2 hourly Thorough investigation (FBC, Retics, U+Es, LFTs, Group and save, LDH, blood cultures if fever, haemoglobinopathy screen if indicated), ADD laxative, thromboprophylaxis, paracetamol, NSAID unless contraindicated IV fluids if insufficient oral intake; Supplemental oxygen if <SO2 <95%	EMSTN guideline page 2
Chest Syndrome	**Prevention! Adequate pain relief, monitor for opioid toxicity, incentive spirometry** Warning signs : chest pain, falling oxygen saturation, SOB Do CXR (look for widespread infiltrate but may be normal) and do ABG on air Liaise with HDU/ ITU transfer Consider transfusion (top up/exchange based on patient factors)	EMSTN guideline page 6
Anaemia	Symptomatic anaemia (SOB, lethargy, pallor) with Haemoglobin usually falling by 25% of baseline or less 20g/l from steady state level Top –up transfusion may be necessary – discuss with haematology Exclude other causes (e.g. parvovirus, bleeding, folate deficiency)	EMSTN guideline page 7
Stroke	Acute ischaemic or haemorrhagic stroke possible Urgent imaging and liaison with local stroke team Thrombolysis indicated as for non-sickle patient Urgent red cell exchange for ischaemic stroke required	
Sequestration	Sudden enlargement of spleen (occasionally liver) with blood pooling resulting in profound anaemia Urgent blood transfusion required	
Abdominal Pain	Investigate cause Ensure adequate analgesia Imaging as guided by clinical features	
Priapism	If prolonged can be medical emergency (exercise, warm bath can help) Analgesia Early discussion with urology if >2hours, may need to aspirate Alpha adrenergic blocker e.g. etilefrine may help Acute transfusion therapy probably not helpful	EMSTN guideline page 8
Sepsis	Take blood cultures and MSSU, other cultures if symptoms Identify cause and treat within local guidance Low threshold for antibiotics and suspend penicillin V if on broad spectrum antibiotics Consider osteomyelitis in any febrile patient with swollen painful limb: Xray may not be helpful especially initially. MRI may be required	
Renal Complications	Check renal function in any acute presentation If painless haematuria, consider papillary necrosis (pain only if accompanied by obstruction) Us may be helpful, otherwise CT. If persistent, bladder irrigation may be helpful	
Vision Loss	Any acute symptoms should be seen urgently - eye casualty	