Guidelines for the Management of Adult Patients with Sickle Cell Disease

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS :
All trained staff – medical and nursing

Lead Clinician(s)

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Key amendments to this guideline

Date	Amendment	By:
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Section 1
INTRODUCTION

Sickle cell disease is an inherited disorder of haemoglobin production due to the presence of haemoglobin S and absence of Haemoglobin A. Haemoglobin S is formed due to a mutation causing an amino acid substitution, glutamine to valine at position 6 of the β globin chain of haemoglobin. The sickle haemoglobin molecule is of low oxygen affinity but has a tendency to polymerise. This results in sickling of red cells particularly in conditions of dehydration, hypoxia and cold.
Sickled red cells have a shortened life span (16-20 days as opposed to 120 days) and cause a *haemolytic anaemia*. They adhere, with white cells, to the endothelium of the microcirculation causing micro vascular occlusion. This can result in *infarction and damage to almost any organ*. Endothelial damage in large vessels, complicated by vasoconstriction and nitric oxide deficiency (due to the presence of free haemoglobin from haemolysis) can result in conditions such as *pulmonary hypertension and stroke.*

Patients at risk include those with ethnic backgrounds from Africa, India, the Mediterranean, South and Central America, the Caribbean and the Middle East.

These guidelines cover patients with sickle cell disease that is;

- Homozygous sickle cell anaemia (Hb SS) – approx 70% of patients. These patients will have No Haemoglobin A on haemoglobin electrophoresis.

- Compound heterozygotes for Hb S and Hb C (Hb SC) – most of the rest of the patients. These patients will have Hb S and Hb C in roughly equal proportions on haemoglobin electrophoresis and No Haemoglobin A.

- Compound heterozygotes of Hb S and β° thalassaemia (Hb S/B° thal), Hb S and B+ thalassaemia (Hb S / β+thal) and very rare conditions such as (Hb S/ Hb Lepore), (Hb S/ Hb D Punjab) and (Hb S/ Hb O Arab)

These guidelines DO NOT COVER patients with sickle cell trait (Haemoglobin AS) These patients have inherited a normal Haemoglobin A gene from one parent and the abnormal Haemoglobin S gene from the other. These patients will have a positive sickle screening test and haemoglobin electrophoresis is likely to show about 30% Haemoglobin S and about 70% normal Haemoglobin A. They may have a borderline anaemia. Symptoms due to sickling occur very rarely in such patients and only in extreme circumstances. Such patients presenting in pain should NOT be regarded as having symptoms of sickle cell disease and an alternative cause should be found.

These guidelines do not cover patients with Hb S/ hereditary persistence of fetal haemoglobin, which should be managed as for sickle cell trait.

This guideline covers the acute care of adult patients presenting with and admitted with the complications of sickle cell disease. It does not aim to cover the specialist long term chronic care of these patients.

Section 2
STAFF COMPETENCIES

These guidelines are intended for the use of all **trained** staff (medical and nursing) on the wards, in A+E and in MAU and ITU.

Individual practitioners remain responsible for any prescriptions that they write or drugs they administer.

All persons making observations should be competent to do so, including assessment of pain and sedation as well as respiratory rate, oxygen saturation, temperature, pulse and blood pressure. Competency should include knowledge of when escalation to a more senior member of staff (medical / nursing) is required.

This document is intended for guidance only. Each patient still requires personalised assessment; appropriate amendments should be made accordingly and if necessary after discussion with the on call Haematologist.

Section 3

TYPES OF SICKLE CELL CRISIS

Painful – sickled red cells cause vaso-occlusion and infarction often in bones

Chest syndrome – this is an acute life threatening medical emergency usually due to combinations of vaso-occlusion / pulmonary infarction and infection

Abdominal crisis.
Sequestration – sequestration of sickled red cells in the liver (and in young children the spleen) can cause rapid life threatening anaemia.
Mesenteric
Acute intrahepatic cholestasis
Also see “Acute Abdomen” below

Aplastic crisis – often due to infection such as parvovirus producing transitory arrest of haematopoiesis. In patients with sickle cell disease there is very rapid red cell turnover with dramatically reduced red cell survival so a transitory loss of production can result in rapidly worsening anaemia.

Priapism

Neurological crisis and stroke – large vessel damage is caused by repeated endothelial damage due to adherent sickle cells, complicated by vasoconstriction and nitric oxide deficiency

Hyperhaemolysis very rare – occurs about 1 wk post transfusion with haemolysis of transfused *and* patients own blood.

Dactilitis – often the first manifestation of sickle cell disease in infants and small children

Section 4
RAPID ASSESSMENT OF PATIENTS WITH SUSPECTED SICKLE CELL CRISIS

This will be done in A+E or MAU

Observations should be done every 30 minutes until the pain is controlled then hourly for 6 hours if a strong opiate has been given and should record:

- Respiratory rate
- Oxygen saturation
- Pain score
- Sedation score
- Pulse and blood pressure
- Temperature (4hourly)
- Fluid balance – **commence chart on every patient**
- (Neurological observations if appropriate)

Initial assessment should look for;

- The cause of the pain
- Infection
- Dehydration
- Acute chest syndrome (fever, tachypnoea, chest pain, hypoxia, chest signs)
- Severe anaemia
- Abdominal crisis. Gall stone disease. (See below – acute abdomen)
- Enlargement of liver or in children the spleen.(may indicate hepatic / splenic sequestration)
- Neurological events
- Priapism

Patients should initially be triaged to the resuscitation room and the CONSULTANT HAEMATOLOGIST on call informed IMMEDIATELY if the patient has;

- suspected acute chest syndrome / oxygen saturation on air <90%,
- Hb <5,
-organ involvement,
-neurological deficit,
-priapism

A haematologist should be involved early in the management of patients with markers of severe disease such as;

-chest pain, including the spine
-oxygen saturations on air <90%
-tachypnoea
-tachycardia
-abdominal pain with distension or a silent distended abdomen
-vomiting and altered bowel habit
-pregnancy of >12 weeks

Section 5
INVESTIGATION OF PATIENTS WITH SICKLE CELL DISEASE.

All patients should have ;

- Full blood count
- Reticulocyte count
- Renal function
- Bilirubin

Most patients will need;

- septic screen –blood cultures, MSU, throat swab (all patients with temp > 38 degrees C)
- Chest x-ray (any chest symptoms or signs, fever >38C, hypoxia)
- CRP
- Liver function tests
- Group and Save

Also consider if clinically indicated;

- Arterial blood gases (Sat <92% or chest syndrome suspected)
- Amylase
- Parvovirus serology (reticulocytopenia – if present discuss with haematologist)
- Abdominal ultrasound (disturbed liver function, organomegaly)
- Brain imaging (fit, stroke, severe headache, neurology- discuss with radiologist re use of contrast as some types cause / worsen crisis)
- Limb radiographs (not usually needed -only if trauma / osteomyelitis suspected or persistent unexplained limb swelling. Sickling itself can cause localised painful swelling)

Sickle cell disease is a chronic haemolytic anaemia so patients have raised unconjugated bilirubin levels, (usually in the region of 20 – 50micromol/l when not in crisis), raised LDH, and a significant reticulocytosis.

Patients often have a raised baseline white cell count (even correcting for nucleated red cells) and a mildly raised platelet count.

Hb SS patients usually run a haemoglobin between 6.5 and 10g/dl;(a little higher in the other forms of sickle cell disease). A patient may know their baseline haemoglobin.

A normal or low reticulocyte count is a cause for concern as it may represent marrow aplasia with the risk of rapid profound anaemia. This should be discussed with a haematologist.

Section 6
INITIAL MANAGEMENT OF PATIENTS WITH SICKLE CELL CRISIS

PAIN – AIM first dose analgesia within 30 minutes of presentation. Pain controlled within 60 minutes

Consider;
What analgesia the patient has already taken and whereabouts this falls on the WHO analgesic ladder
Is this pain typical of their usual sickle pain or is there an alternative explanation.

For moderate or severe pain give morphine 0.1 to 0.15 mg/kg sc (or iv)
Alternatively sc (or iv) morphine Body weight 35-50kg 5mg
Body weight 50-65kg 7.5mg
Body weight 65-100kg 10mg
Also offer regular paracetamol and NSAID (naproxen) unless contra indicated.

For mild pain in patients who have already had analgesia or moderate pain in those who have not had any analgesia, consider a weak opioid and offer regular paracetamol and an NSAID if not contraindicated

Reassess after 30 minutes and consider / offer a further bolus of a strong opioid (or first bolus if not previously given) if the pain is not controlled.

Reassess every 30 minutes until the pain is controlled

Prescribe prn medication for breakthrough, usually 2-4 hourly – strong sc opiate bolus in those previously needing these (although some patients may prefer oramorph)

See pain management below.

OBSERVATIONS

All patients taking strong opioids should be monitored for adverse events. Observations should include respiratory rate, oxygen saturation, pulse and blood pressure and a clinical assessment of sedation score and pain. (Temperature should be monitored 4 hourly initially or as per clinical assessment). An accurate fluid balance chart should be kept. Observations should be performed,

4hourly throughout the patient admission

1-2 hourly if there is a suspicion of deterioration

1 hourly for the first 6 hours after treatment with a strong opioid

At least every 30 minutes if the patient has unstable pain control and is requiring rescue analgesia

IF RESPIRATORY RATE <12 /MIN OR OXYGEN SATURATION FALLS TO <90% OR SEDATION SCORE IS 3 (or persistently 2) NO FURTHER OPIATES SHOULD BE GIVEN AND A DOCTOR CALLED.

WARM

Keep patients warm – cold precipitates crisis

OXYGEN

Oxygen should be given to hypoxic patients / patients who have oxygen saturations below their normal steady state. If a patient's steady state is unknown, oxygen should be given if the oxygen saturation is below 95%. (All patients needing oxygen require admission)

FLUIDS

Give fluids – sodium chloride 0.9% 1 litre over first 3 hours. Oral fluids can also be used. Ensure adequate fluid intake – correct any dehydration and then ensure an intake of at least 60ml/kg/24hrs in an adult patient with normal losses. If oral intake is likely to be insufficient NG or iv routes should be used. Difficult unnecessary cannulation should be avoided. (but need iv access for safety in patients receiving repeated doses of parenteral opiate) In particular cannulation of the veins of the legs and ankles should be avoided because of the risk of leg ulcers and venous thrombosis. Central lines should be avoided because of the risk of thrombosis, unless needed for life saving blood transfusions

ALL patients **MUST** have an **accurate fluid balance chart – even those attending A+E who are not admitted**

ENOXAPARIN

All admitted patients without contraindications should receive thromboembolic prophylaxis with enoxaparin 40mg sc daily. Sickle cell crisis is a prothrombotic condition and patients are at particular risk of thromboembolic complications.

FOLIC ACID

Give folic acid 5mg daily. (Patients would usually be on this already)

ANTIBIOTICS

Antibiotics –patients are hyposplenic and should be on prophylactic antibiotics which should be continued unless infection is suspected. (See trust antibiotic policy)

If infection is suspected, and in all patients with a temperature >38 degrees broad spectrum antibiotics should be started as per the antibiotic policy.

Sickle cell disease patients are hyposplenic and at particular risk of infection with encapsulated organisms such as pneumococcus, haemophilus and meningococcus.

Consider the respiratory and urinary tracts and osteomyelitis as foci of infection. Sickle cell disease patients are also at risk of gram negative sepsis.

A macrolide should be added if chest symptoms are present. (Unless contraindicated).

Occasionally patients may be on iron chelators. These patients are at risk of **yersinia** infection so if diarrhoea is present the chelation should be stopped and patients treated with ciprofloxacin, after discussion with a microbiologist and appropriate blood and stool samples.

BLOOD TRANSFUSION

This is not usually indicated, but in some circumstances can be life saving. (see below)

If the patient is on **hydroxycarbamide** this should be stopped in an acute crisis especially if there is any evidence of neutropenia, thrombocytopenia or reticulocytopenia.

Section 7

COMMON CHRONIC COMPLICATIONS OF SICKLE CELL DISEASE

Hyposplenism – almost universal in Hb SS after early childhood with a risk of overwhelming sepsis.

Bony necrosis and infarction. Osteomyelitis. Necrosis of the femoral and humeral heads.

Pulmonary hypertension and right heart failure. Common in older patients. Chronic sickle lung disease

Gall stones

Renal failure – renal papillary necrosis, glomerulonephritis, renal infarcts, nephrotic syndrome,
Pyelonephritis.

Retinopathy – particularly Hb SC

Leg ulcers.

Section 8
PAIN ASSESSMENT AND MANAGEMENT

(Please use these guidelines in conjunction with the trust guidelines on Acute Pain Control for The Alexandra Hospital and for Worcestershire Royal Hospital)

Patients with sickle cell disease can have pain due to any of the usual medical and surgical causes. Patients should be assessed to determine whether their pain is being caused by an acute painful sickle cell episode or whether an alternative diagnosis is possible.

The patient (or their carer) should be regarded as an expert in their condition. They are often skilled in knowing exactly how their crises develop and can say whether the pain is typical of their usual sickle pain or not. Notice should be taken if a patient says that their pain is unusual /atypical or that this problem is “different”, and further advice sought.

Discussion with the patient / carer should include the planned treatment regime for this episode, treatment received during previous episodes, any concerns they may have about the current episode and any psychological or social support they may need.

The pain of sickle cell crisis is genuine, can be excruciating and can be greater than that of childbirth.

A pain chart should be commenced and pain, respiratory rate, sedation score and oxygen saturations measured at least every 30 minutes interval until the patient is stable and pain controlled.

Analgesia should be given within 30 minutes of reaching hospital and effective analgesia achieved within 60 minutes

Primary analgesia

Ensure drug dosages and routes of administration are suitable for the severity of the pain and age of the patient.

Generally consider the WHO analgesic ladder, commencing at the step above what the patient has already received.

Mild pain	non-opioid +/- adjuvant	paracetamol, naproxen
Moderate pain	weak opioid (or low dose strong opioid) +/- non-opioid +/-adjuvant	co-codamol (8/500) / tramadol /codeine / dihydrocodeine
Severe pain	strong opioid +/- non-opioid +/- adjuvant	morphine / diamorphine

Ask about and take into account any analgesia the patient has already taken for this episode and refer to their card detailing their individual pain management strategy if they carry one.

Offer a bolus dose of a strong opioid for acute painful sickle cell episodes to all patients presenting with severe pain and all patients with moderate pain who have already had some analgesia.

Consider a weak opioid as an alternative to a strong opioid for patients presenting with moderate pain who have not yet had any analgesia.

Offer all patients regular paracetamol and NSAIDs (non steroidal anti inflammatory drugs) in addition to opioid, unless contraindicated

If patients are on regular long acting analgesia eg Morphine Sulphate Slow Release; this can be continued. If sc prn morphine is prescribed then do not prescribe their regular short acting opiates.

Pethidine should NOT be used (except in exceptional circumstances when no alternative exists). It is short acting and its metabolites are renally excreted cerebral irritants causing dysphoria, clonus and seizures. Muscle damage is described after im injection and im bioavailability, particularly if injected into “scarred” muscles, is unpredictable.

Nitrous oxide (Entonox) can be used in the first 30 minutes in hospital to help control severe pain, provided oxygen saturation is normal. It should not be continued after this time because of the risk of neuropathy and megaloblastic anaemia.

Not all patients with simple painful crisis will require admission. A single parenteral injection followed by oral analgesia may be sufficient to control pain in some patients with no other complications. Such patients require a period of observation (e.g. 2-4 hours) to ensure their pain is controlled and there are no complications with respect to the parenteral analgesia. They also require full medical assessment and investigation including full blood count, renal function, reticulocyte count and bilirubin.

After initial pain control the patient should be prescribed a basal level of regular parenteral or oral analgesia with provision for bolus “as required” analgesia if breakthrough occurs.

Patient controlled analgesia (PCA) can be considered if repeated boluses of a strong opioid are needed within 2 hours but should only be used after initial control of pain is achieved using bolus opioids. It should only be used in a clinical setting where the medical and nursing staff are entirely familiar with and trained in its use and protocols in place for safe administration and patient observation. In sickle cell patients pain control is usually better with a low basal infusion rate and high-dose PCA rather than high basal infusion and low dose PCA.

Consider TENS machine if available

<u>Outline of management of acute severe sickling pain in opiate naive adults when oral analgesia not effective.</u>

Rapid clinical assessment

Patients needing repeat doses of parenteral opiates should have iv access.

0.1 mg/kg morphine sc (or iv) repeated every 20-30 min until pain controlled

0.05-0.1mg/ kg morphine every 2-4hours sc/po (or iv)

Also give non opioid analgesia – paracetamol, ibuprofen, naproxen.

Monitor vital signs – respiratory rate, oxygen saturation, sedation and pain every 20-30 minutes until stable and then monitor respiratory rate, oxygen saturation, sedation, pain, temperature pulse and blood pressure every 1 hour for 6 hours then 4hourly. (See "observations" above)

If the patient has severe pain on reassessment, give rescue doses of analgesia at 30 minute intervals – 50% of maintenance dose.

If respiratory rate less than 12/minute omit maintenance analgesia. If severe respiratory suppression /sedation (respiratory rate <8) give naloxone 1mg iv repeated every 2 minutes as necessary.

If adequate pain control is not achieved advice should be sought from the acute pain service / anaesthetists and from the haematology specialist nurse / haematologist on call.

Laxatives should be prescribed routinely for patients on opiates – senna 2-4 tablets daily or sodium docusate (adults only) 100mg bd

Offer antipruritics for opiate induced itch – hydroxyzine 25mg bd.

Offer antiemetics – cyclizine 50mg tds, prochlorperazine

Consider anxiolytics if required in adults – haloperidol 1-3mg po/im bd.

Ongoing management / pain reassessment

See "observations"

Pain should be reassessed regularly (every 20-30 min initially and at least 4 hourly thereafter) using an appropriate tool until satisfactory pain control has been achieved. See appendix 2 and "Trust Guidelines on Acute Pain Control". Also use phrases such as; How well did that last painkiller work?" and "Do you feel that you need more pain relief?"

If a strong bolus opioid was not used initially but the patient remains in severe pain at 30min strong bolus opioid should then be used

If the patient does not respond to standard treatment for acute painful sickle cell episode, reassess them for a possible alternative diagnosis.

Encourage the patient to use their own coping mechanisms for dealing with acute pain – eg relaxation techniques.

Complications of acute painful sickle cell episodes can develop at any time during admission. Be vigilant for these especially

Chest crisis – increasing hypoxaemia / oxygen saturation <95%, chest pain, fever, abnormal respiratory signs and symptoms.
Acute stroke
Aplastic crisis
Infections
Osteomyelitis
Splenic / hepatic sequestration

Reduce analgesia after 2-3 days if pain controlled / improving. Switch to oral medications.

Section 9
BLOOD TRANSFUSIONS

The two indications for transfusion in sickle cell disease are;

1) To correct anaemia and so improve the oxygen carrying capacity of blood

2) To treat or prevent the occurrence of painful/vaso-occlusive or sequestration complications by lowering the percentage of Hb S relative to Hb A

Transfusions are not usually indicated for anaemia until the haemoglobin falls below 5g/dl (HbS carries oxygen more efficiently than HbA) but each patient should be assessed individually (eg patients with cardiopulmonary disease).

It is usual for haemoglobin to fall 1-2g/dl in an uncomplicated painful crisis but transfusion is not routinely indicated.

Consider the causes of acute anaemia; (what is the patients usual baseline haemoglobin?)
- Blood loss
- Transient red cell aplasia (human parvovirus B19)
- Sequestration syndromes
- Acute haemolysis (including hyperhaemolysis, acute and delayed transfusion reactions, malaria G6PD deficiency and sickle crisis)

Top up transfusion is indicated for acute anaemia with reticulocytopenia and for acute splenic sequestration. The threshold will depend on the clinical state of the patient.

Exchange transfusion (or top up transfusion) will usually be required for chest crisis and acute neurological / cerebrovascular events and may well be needed in severe sepsis, acute hepatic sequestration, acute multi- organ failure, stuttering priapism, pre operatively and in progressive intrahepatic cholestasis.
In a patient with Hb SS an exchange transfusion would usually aim to reduce the Hb SS to < 30% but keep Hb <10g/dl. Each patient will need individual assessment. All patients in whom exchange transfusion is being considered should be discussed with the Consultant Haematologist.

Some patients may be on a regular transfusion regime for the management of the chronic complications of sickle cell disease e.g. stroke in children or during pregnancy. Transfusion in these patients should be discussed with their usual physician or the local haematologist.

If blood transfusion is required blood should be matched for rhesus genotype and Kell negative and should be sickle negative. (Unless the need for life saving transfusion is so urgent that this is not possible). Standard ABO matching is required. Red cell alloimmunisation is relatively common in sickle cell patients

<u>Any patient in whom transfusion is being considered should be discussed with a haematologist.</u>

Section 10
ACUTE CHEST CRISIS

This is an acute life threatening emergency and can develop at any time during an admission and progress rapidly.

Acute chest crisis is defined by the National Acute Chest Study Group in the USA as a new infiltrate consistent with consolidation and at least segmental in size, accompanied by at least one of: chest pain, fever > 38.5 degrees C, tachypnoea, wheezing or cough. X-ray changes often lag behind clinical features however and **hypoxemia should always be taken very seriously.**

All cases should be discussed with the Consultant Haematologist on call and will usually need managing in conjunction with the intensive care outreach team, HDU/ ITU and advice from tertiary care at the City Hospital Birmingham.

Clinical features – early recognition is vital

Pain in chest wall, upper abdomen, and/or thoracic spine. ACS may be a presenting feature or may develop after a painful vaso-occlusive crisis affecting limbs.
Signs of lung consolidation, usually bilateral and generally starting at the bases. Upper and middle lobe consolidation, without basal changes is suggestive of chest infection rather than sickle acute chest syndrome.
Fever
Tachypnoea
Tachycardia
Cough may be a late symptom (dry or fluorescent yellow sputum)
Physical signs may precede X-ray findings

Special investigations

Arterial blood gases on air
Chest X-ray
Blood cultures, sputum cultures, respiratory serology (including Chlamydia, mycoplasma and parvovirus) nasopharyngeal aspirate for virology.(RSV Flu A and B, para-flu, metapneumovirus, adenovirus.)
Monitor saturations on and off inhaled oxygen
Ensure that a Group and Save sample is sent
(CT of the chest and V/Q scanning are not helpful in the acute setting but CT-PA is recommended if there is a high suspicion of pulmonary embolism)

Management

Contact Critical Care Services outreach team, and contact Haematologist on call
If significant hypoxia then consider CPAP. Monitor patient closely- oxygen saturations at least hourly
Early top up transfusion should be considered, but urgent exchange transfusion will be needed if there is worsening hypoxia and respiratory distress. This should be discussed with the Haematology Consultant.
In severe cases ventilation may be required.
Consider precipitants, opiates, PE, fluid overload as well as infection

IV fluids: care to avoid fluid overload
Broad spectrum antibiotics and a macrolide (and antivirals if suspicion of H1N1 flu)
Incentive spirometry
Nebulised salbutamol 2.5 mg four times per day
Adequate analgesia
Monitor markers of severity – respiratory rate, hypoxia, multilobular involvement, neurological symptoms, thrombocytopenia and worsening anaemia.
Refer to physiotherapist

<u>High risk situations for the development of ACS</u>

Post-operatively
Patients with rib pain
Third trimester of pregnancy

Encourage early mobilisation, chest physiotherapy, and incentive spirometry

Patients who have >2 ACS should be offered hydroxycarbamide.

Section 11
PRIAPISM

This can lead to long term erectile dysfunction.

Two types :

1. Stuttering – usually self limiting in <1 hour. A cluster of attacks can precede an acute episode.

2. Acute – this is a urological emergency and urgent urological management should be sought from the on call Urologist and Haematologist.

Evaluate for precipitating causes (alcohol, sildenafil, substance abuse / psychotropic drugs, infection, trauma, alpha blockers) and ability to pass urine.

Treat with fluids and analgesia – empty bladder early and regularly

Urological treatment can be with intracorporeal aspiration of blood with penile irrigation /sterile saline lavage. If this is unsuccessful, injection with a selective alpha 1 adrenergic agonist, such as phenylephrine every 5 - 10 minutes can be considered. (Careful blood pressure and pulse monitoring in resus) This can be repeated several times per episode.

(NOTE – alpha adrenergic agonists can cause HYPERTENSIVE CRISIS so should only be used under expert guidance and supervision)

Exchange transfusion can be considered if other measures fail but response is variable. It can be used for stuttering priapism to help prevent an acute event but tends to be less successful in resolving an acute episode.

Operative measures can be considered but are almost always associated with erectile dysfunction

Patients should be discharged with an alpha adrenergic agonist for prophylaxis.

Section 12
NEUROLOGICAL CRISES AND STROKE

Patients with new neurological signs or acute stroke (which can be ischaemic or haemorrhagic) should be discussed with the Consultant Haematologist on call.

There is concern that some types of contrast media can facilitate sickling – this should be discussed with the radiologist before contrast is used in imaging. Acute neurological symptoms require urgent imaging.

Urgent exchange (or top up) transfusion will usually be required for patients with acute stroke and before angiopathy, aiming to reduce HbS to <20% over 2-3 days, taking care to avoid hypovolaemia or haemoglobin greater than 12g/dl and keep haematocrit <0.35 (to avoid hyperviscosity which can cause seizures)

Haemorrhagic stroke should be managed in conjunction with the neurosurgical centre in the usual way.

Thrombolysis is not recommended for ischaemic stroke but aspirin or clopidrogel should be used if ischaemic stroke occurs in the absence of significant intracranial vasculopathy.

Consider venous sinus thrombosis (anticoagulation and thrombolysis can be considered if general measures are insufficient).

Consider moyamoya disease, vascular malformations, aneurysms, carotid critical stenosis and dissections

Section 13
OSTEOMYELITIS

Difficult to differentiate from painful crisis and bony infarction as both present with local tenderness, warmth, swelling, fever and a raised white cell count. Painful crisis is 50 times more common but sickle cell patients are particularly susceptible to osteomyelitis due hyposplenism and the presence of infarcted / necrotic bone

Positive blood cultures are the most useful diagnostic test. (Commonly salmonella, (atypical types) staphylococcus aureus, gram negative enterobacteria.)

Plain X-rays are non specific early on but later may show lucent areas. Bone scans and leukocyte scans do not discriminate infection from infarction. Gadolinium enhancement may help diagnosis. Ultrasound showing fluid depths >4mm is associated with osteomyelitis MRI can be useful.

If clinical suspicion is high antibiotic treatment can be used whilst awaiting cultures. Investigate if there are ongoing bony symptoms not settling after 1-2 weeks

Osteomyelitis should be treated for 6 weeks with antibiotics – discuss with microbiologist / refer Trust guidelines (consider above organisms).

The opinion of an orthopaedic surgeon should be sought.

Section 14
ACUTE ABDOMEN

Surgical opinion should be sought early, particularly if gallstone related complications are suspected.

Causes of abdominal pain include;

- Mesenteric syndrome -vaso-occlusion in the mesenteric circulation (Pain, no peritonism, silent bowel sounds, often associated with bone pain and maybe distended loops of bowel or fluid levels on abdominal X-ray. May mimic acute surgical abdomen. Managed supportively. Nil by mouth / ivi / NG / analgesia. Monitor girth hourly)
- Cholelithiasis / cholangitis / gall bladder disease / gall bladder empyema and pancreatitis (70% of adults with sickle cell disease have gall stones) These are managed in the usual way.
- Constipation – common on opiates
- Pulmonary causes
- Intra abdominal abscess
- Hepatic infarction / abscess / sequestration / acute intra-hepatic cholestasis (see below)
- Splenic infarction / sequestration (see below)
- Renal or hepatic vein thrombosis
- **All the usual causes** of acute abdomen found in non sickle cell disease patients!

All patients for whom surgery is considered should be discussed with the Consultant Haematologist on call. These patients are at increased anaesthetic risk and may need measures such as pre operative exchange transfusion.

Splenic and hepatic sequestration

Splenic sequestration can develop in hours with left upper quadrant pain and tender rapidly enlarging splenomegaly with a drop in haemoglobin of 2g/dl from baseline. It causes profound anaemia and hypovolaemic shock and is often associated with sepsis, particularly due to pneumococcus or haemophilus. It is more common in children, and patients with SC disease as they are less likely to have undergone autosplenectomy. Mortality is high in children.

Hepatic sequestration can cause right hypochondrial pain, abdominal distension, acute tender hepatomegaly, a fall in haemoglobin in the absence of blood loss, rising bilirubin

(predominantly conjugated,) a mild rise in transaminases and alkaline phosphatase. It is often associated with infection eg salmonella

Patients with acute anaemia / hypovolaemia due to hepatic / splenic sequestration should be resuscitated with fluids and will usually require cautious blood transfusion to baseline haemoglobin, particularly those with splenic sequestration where circulatory collapse is more common; (but care must be taken to ensure the haematocrit does not rise excessively, causing hyperviscosity as sequestered red cells return to the circulation.) Commence broad spectrum antibiotics. A good reticulocyte response is useful to differentiate sequestration from aplastic crisis. Monitor carefully for respiratory signs indicative of acute chest syndrome.

These patients should be discussed with the Consultant Haematologist on call.

Acute intrahepatic cholestasis

Severe hyperbilirubinaemia associated with fever and hepatic pain in the absence of demonstrable stones due to intrasinusoidal sickling, kupffer cell hyperplasia and erythrophagocytosis.
Severity is variable. It can be drug induced.

Patients can develop fever, abdominal pain, hepatic encephalopathy and a severely raised bilirubin with raised alkaline phosphatase and variable elevation of transaminases, thrombocytopenia and renal impairment..

Treat with analgesia (care with opioids), hydration, antibiotics and in severe cases with exchange transfusion.

Monitor for mesenteric and sequestration crisis.

Section 15
PREGNANCY

All pregnant patients should be discussed with the Consultant Haematologist on call and the obstetrics team – Crises in these patients carry substantial risk for both mother and baby.

Please also refer to trust guidelines on the management of sickle cell patients during pregnancy.

Section 16
ONGOING CARE

Sickle cell disease patients with severe and / or complicated problems should be managed in conjunction with advice from the sickle cell disease specialist centre at City Hospital in

Birmingham. If necessary patients will be transferred as in patients for tertiary care at City Hospital.

After initial assessment and management in A+E /MAU patients admitted with sickle cell crises or the complications of sickle cell disease should be referred to the Haematology Specialist Nurse (who will liaise with the on call Haematologist) and transferred to Laurel 3 ward (for patients at WRH) or MSSU - male / female MAU(for patients at Alex) for their continuing care. At weekends the on call Consultant Haematologist should be notified of the patient's admission.

On discharge all patients (or their carers) should be provided with information on how to continue to manage the current episode and any potential side effects of the treatment they have received. They should also be advised how to obtain specialist support and any additional medication they may need.

On discharge from hospital all patients should have a follow up appointment after about six weeks (earlier if indicated) with the consultant who is responsible for long term care of their sickle cell disease.

All patients with sickle cell disease should have a named specialist responsible for their care. For patients in Worcestershire this will be one of the consultant haematologists in the trust with tertiary care provided by the regional specialist "Sickle Cell and Thalassaemia Centre"(SCAT) at City Hospital in Birmingham. For all Birmingham patients this would usually be the centre at City Hospital directly (although occasional patients are seen at Heartlands and the QE). If patients from other geographical areas have no such consultant they should be referred to their local haematologist for continuing care.

Section 17
MONITORING TOOL

STANDARDS	%	CLINICAL EXCEPTIONS
Analgesia should be given within 30 minutes of reaching hospital	100%	None
All patients should be offered a bolus of a strong opioid if they have severe pain or if they have moderate pain and have previously received analgesia	100%	None
All patients should have observations measuring respiratory rate, oxygen saturation, pulse, blood pressure and temperature at presentation .	100%	None
All patients should be offered paracetamol, NSAIDS and, if on opiates, laxatives unless there are contraindications	90%	Patients with contra indications
All patients should have their pain assessed at presentation and every 30 minutes thereafter until satisfactory pain control is achieved	100%	None

Section 18
REFERENCES

British Committee for Standards in Haematology General Haematology Task Force. Sickle Cell Working Party – Guideline for the management of the acute painful crisis in sickle cell disease. British Journal of Haematology, 2003, vol 120, 744-752

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P.S. Swerdlow. Red Cell Exchange in Sickle Cell Disease. American Society of Hematology. Educational Program. Hematology 2006 48-51

NICE guidance Sickle Cell Acute Painful Episode. Management of an acute painful sickle cell episode in hospital. June 2012

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S Pancham Protocol for the Management of adult Patients with Sickle Cell Disease. Sandwell and West Birmingham Hospitals NHS Trust. 2011.

NHS England 2013/14 NHS Standard Contract for Specilised Services for Haemoglobinopathy Care. (All Ages) Section B Part 1 Service Specifications

Section 19
CONTRIBUTION LIST

Key individuals involved in developing the document

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Circulated to the chair of the following committee's / groups for comments

Name	Committee / Group
Nick Hubbard	Medicines Safety Committee
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Appendix 1

Table 1. **Suggested protocol for Manual red cell exchange in adults** – see ref.

A. Calculate exchange volume as 1.5 red cell volumes.

B. Red cell volume = patient haematocrit × total blood volume.

- Assume total blood volume is 70 ml/kg if over 20 kg, (85 ml/kg if under 20 kg)
- Each standard unit packed cells has a red cell volume of ~200 ml

C. Perform adult manual exchange as follows:

- Bleed 500ml simultaneously infusing 500ml saline
- Bleed 500ml and then infuse 2 units packed red cells
- Repeat steps 1 and 2 until volume of packed cells administered is equal to planned red cell exchange volume (up to three or even four repeats for large adults)

If patient has a starting haemoglobin close to or more than 10g/dl, this protocol may result in significantly higher haemoglobin after fluid equilibration post exchange. The red cell volume withdrawn in the two 500ml bleeds is less than the red cells administered by the two units of blood (by the amount the patient's haemoglobin is less than normal). You may wish to consider a 500 ml bleed at the end or alternate infusing 1 unit instead of 2 units in the second (and fourth if needed) cycle of 3 steps. While this difference is even greater for those with lower haemoglobins, such patients are less likely to exceed a haemoglobin of 10g/dl by the end of the procedure.

Appendix 2

Assessment of pain and sedation (see also trust guidelines on acute pain control)

Pain severity on movement	Code
None	0
Mild	1
Moderate	2
Severe	3

Severe pain at rest should be coded 3

Sedation level	Code
Awake	0
Drowsy	1
Sleeping but rousable	2
Difficult to rouse	3

Sedation level should **also** be added to the PARS score using the alternative numerical scoring

Awake	0
Responds to Voice	1
Responds to Pain	2
Unresponsive	3

Supporting Document 1 – Checklist for review and approval of key documents

This checklist is designed to be completed whilst a key document is being developed / reviewed.

A completed checklist will need to be returned with the document before it can be published on the intranet.

For documents that are being reviewed and reissued without change, this checklist will still need to be completed, to ensure that the document is in the correct format, has any new documentation included.

1	Type of document	Clinical Guideline
2	Title of document	Management of Adult Patients with Sickle Cell Disease
3	Is this a new document?	Yes ☐ No ☒ If no, what is the reference number WAHT-HAE-012
4	For existing documents, have you included and completed the key amendments box?	Yes ☐ No ☐
5	Owning department	Haematology
6	Clinical lead/s	Elizabeth Maughan
7	Pharmacist name (required if medication is involved)	
8	Has all mandatory content been included (see relevant document template)	Yes ☒ No ☐
9	If this is a new document have properly completed Equality Impact and Financial Assessments been included?	Yes ☐ No ☐
10	Please describe the consultation that has been carried out for this document	
11	Please state how you want the title of this document to appear on the intranet, for search purposes and which specialty this document relates to.	
Once the document has been developed and is ready for approval, send to the Clinical Governance Department, along with this partially completed checklist, for them to check format, mandatory content etc. Once checked, the document and checklist will be submitted to relevant committee for approval.		

Implementation

Briefly describe the steps that will be taken to ensure that this key document is implemented

Action	Person responsible	Timescale

Plan for dissemination

Disseminated to	Date

1	**Step 1 To be completed by Clinical Governance Department** Is the document in the correct format? Has all mandatory content been included? Date form returned 29/01/2013	Yes ☒ No ☐ Yes ☒ No ☐	
2	Name of the approving body (person or committee/s)	Haematology Directorate Meeting	Medicine Safety Committee
	Step 2 To be completed by Committee Chair/ Accountable Director		
3	Approved by (Name of Chair/ Accountable Director):	Elizabeth Maughan	Alison Smith
4	Approval date	??/01/2013	Date to be added

Please return an electronic version of the approved document and completed checklist to the Clinical Governance Department, and ensure that a copy of the committee minutes is also provided.

Office use only	Reference Number	Date form received	Date document published	Version No.