Management of Children with Sickle Cell Disease

University Hospitals of Leicester NHS NHS Trust

EMSTN East Midlands Sickle Cell and Thalassaemia Network

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1 INTRODUCTION AND WHO THIS GUIDELINE APPLIES TO

Concise guideline for overall management of paediatrics patients with Sickle Cell Anaemia

1 Sickle cell disorders are a heterogeneous group of disorders affecting patients in whom haemoglobin S is the major haemoglobin. They include haemoglobin SS, SC and S/beta thalassaemia

2 This clinical policy has been compiled by the local paediatric haemoglobinopathy team within the East Midlands Sickle Cell and Thalassaemia Network (EMSTN). It has been formulated following reviews in service, based on current practice and research including published standards in the management of children with sickle cell disease

3 It is intended for the guidance of in and out-patient management. Cases need to be assessed individually and the management tailored appropriately. The opinion of the local paediatric haemoglobinopathy team should be sought where necessary

Relates to paediatric haematology teams, paediatric emergency medicine, paediatric medicine and specialties (nephrology, urology, microbiology, endocrinology, surgery, gastroenterology, anaesthesia, orthopaedics, ophthalmology, ENT)

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2. DEFINITIONS

Haemoglobinopathy	A group of inherited conditions where the pathology relates to abnormalities in haemoglobin production or function. Includes haemoglobin variants and thalassemias
Sickle cell disease	This encompasses a number of genotypes including Hb SS, Hb SC, Hb S/beta thalassaemia and some rarer compound heterozygote states where HbS dominates and results in a clinically significant condition
Child	For the purposes of this policy a child is a person less than 16 years old
Adolescent	This includes teenagers and young adults aged up to 18 years. Some of these will be managed in the paediatric service and some in adult service
PCA	Patient controlled analgesia
PEEP/CPAP	Positive end-expiratory pressure / Continuous positive airway pressure

3. ARRANGEMENTS FOR EMERGENCY ASSESSMENT, ADMISSION AND SPECIALIST ADVICE

1. Patients should have open access to an acute care facility.
2. Emergency patients should be booked through reception and rapidly assessed & triaged.
3. A record of observation and clinical assessment should be made.
4. Unwell patients will be managed in the resuscitation suite according to trust paediatric resuscitation guidelines.
5. Paediatric attending team will be informed of acute presentation for urgent review.
6. All patients will be rapidly moved to a bed/cubicle for prompt treatment.

7. Medical and nursing staff will identify individual patient care plan to access treatment plan and follow guidance.

8. For acute pain crisis, analgesia if required will be administered according to Appendix 4 aiming for first dose within 30 minutes of presentation.

9. A decision to deviate from the pathway should only be made following discussion with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call).

10. Prompt medical assessment will follow including recording of presenting problem and documentation of treatment plan.

11. Required analgesia and other urgent medication including antibiotics will be prescribed on medical drug chart to avoid delay in administration of subsequent doses. If required, the second dose of analgesia will be administered BEFORE patient is moved to the acute inpatient ward.

12. The admitting paediatric team remain responsible for the inpatient episode until the next working day. The paediatric haemoglobinopathy team should be informed of their admission and asked for advice.

13. Unwell patients will be prioritised on the ward round for review.

4. GUIDELINES FOR MANAGEMENT OF ACUTE COMPLICATIONS

Routine Baseline Investigations:

- FBC, reticulocyte count
- U+Es, LFTs, LDH
- CRP
- G+S
- Red cell phenotype (if not known)

In older children presenting with an uncomplicated vaso-occlusive sickle cell crisis, a finger prick test for FBC may be done in the first instance. Note however, all patients on hydroxycarbamide and chelation therapy must have routine baseline investigations as above. Other tests may be indicated based on presentation.

- CXR (respiratory symptoms/signs)
- Urine dipstick/culture, blood, throat, nose, sputum, stool, wound, CSF culture, NPA (as dictated by symptoms)
- Urine pneumococcal antigen
- Sputum/induced sputum for atypical pneumonia PCR & Mycoplasma serology(needs discussion with a microbiologist – patients with respiratory symptoms/signs)
- Parvovirus serology (IgM) / DNA (pallor/falling Hb/low reticulocyte count)
- CT/MRI/MRA head (CNS symptoms/signs)
- Arterial/capillary blood gases (respiratory distress/metabolic compromise)
- Hb S% (acute chest syndrome or stroke)
- Yersinia stool culture for patients on desferrioxamine with diarrhoea/abdominal pain (request form must specifically state for Yersinia culture to ensure correct incubation)
- Serum amylase (abdominal symptoms/signs)
- USS abdomen (abdominal symptoms/signs, features of girdle syndrome, sequestration, cholecystitis)

- USS limb/MRI limb/limb or joint x-ray (suspected osteomyelitis)

Admission to hospital (please inform paediatric haemoglobinopathy team)

The following are indications for admission to hospital:

- Persistent temperature
- Pallor, lethargy, malaise, abdominal distension
- Severe pain requiring opiate analgesia
- Symptoms and signs suggesting acute chest syndrome, acute cerebrovascular event, sequestration syndrome, aplastic crisis and fulminant priapism

Discharge from hospital

Prior to discharge all cases must be discussed with the paediatric haemoglobinopathy team. Appropriate follow up should be arranged. A short supply of analgesia should be made available.

Follow up options

- Inform paediatric haemoglobinopathy team to arrange early outpatient appointment if required.
- All discharges out of hours must be notified to the paediatric haemoglobinopathy team the following day by email.

5. MANAGEMENT OF COMPLICATIONS

Acute Pain Crisis

1. This is the most frequent complication of sickle cell disease and a common reason for presentation to hospital. Typically the child will present with limb, back or chest pain. A trial of simple analgesia may have been instituted by the family. An enquiry into this as well as potential precipitating factors should be made e.g. coryzal symptoms, dehydration.

2. The mainstay of the management of sickle cell crisis is supportive and includes:
   - Pain relief
   - Fluid replacement (in accordance with trust paediatric IV fluids guideline)
   - Oxygenation

3. Pain Management and PCA - please see Appendix 4 and Guideline for the care of children and young people (under 18yrs) requiring morphine,fentanyl and ketamine and morphine patient controlled analgesia (PCA), nurse controlled analgesia (NCA) & contnuous morphine infusion. http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Patient%20(PCA)%20and%20Nurse%20Controlled%20Analgesia%20(NCA)%20and%20Continuous%20Morphine%20Infusion%20UHL%20Childrens%20Hospital%20Guideline.pdf

Fluid Replacement

4. **Rationale:** Many patients with sickle cell disorders have reduced tubular concentrating ability. Continued fluid loss without adequate replacement causes a reduction in plasma volume with an increased blood viscosity and aggravation of sickling.

5. Children with sickle cell disease need individualised fluid regimes. They are often dehydrated and will need additional fluids; conversely over zealous fluid replacement may make the situation worse by precipitating cardiac failure.

6. The oral/enteral route is always preferred. However, in those who are unable to tolerate this, IV fluids may be required in accordance with trust paediatric IV fluid guidelines.

7. Intravenous therapy should be stopped once the patient is stable and can tolerate oral/enteral fluids.

8. Adequate oral intake should be documented.

Infections

9. Sickle cell patients are particularly susceptible to severe overwhelming bacteraemia..

10. Important organisms to consider are *Streptococcus pneumoniae*, *E coli* and *Salmonella* species. The use of prophylactic penicillin has decreased the incidence of pneumococcal infections.

11. Always look for a focus of infection when the patient is febrile and organise cultures accordingly.

12. In suspected sepsis, hydroxycarbamide and chelation therapy should be reviewed due to the risk of cytopenia.

13. Stop hydroxycarbamide if febrile neutropenia or bleeding with thrombocytopaenia.

14. Dose reduction of certain antibiotics should be considered if the patient has renal impairment. Please discuss with a pharmacist if in doubt.

15. Any child with a **sequestration syndrome, chest syndrome, or septic, must receive IV antibiotics:**

    - Please refer to **Sepsis UHL Childrens Hospital Guideline.**
    - Duration of treatment as per local guidelines and according to microbiology results.

16. Any child with two temperatures of 38.0°C or one at 38.5°C, who appears mild to moderately ill should receive IV antibiotics:

    - Usually IV ceftriaxone or cefotaxime (for dosage see BNFC)
    - Duration of treatment as per local guidelines and according to source of infection and microbiology results

17. If signs of chest infection, discuss with microbiology additional antibiotic to cover atypical pneumonia including Mycoplasma.

18. Patients who are clinically well and are afebrile should continue penicillin prophylaxis. If the child then enters either category 5.15 or 5.16, treat as above.

Treatment for osteomyelitis

19. If the decision is taken to treat for osteomyelitis, antibiotics should be chosen to cover *Salmonella, Streptococcus* and *Staphylococcus spp*. Always discuss cases with the microbiology team.

20. Consider insertion of PICC line if the patient requires prolonged IV therapy.

21. The patient may require surgical debridement.

    Under no circumstances must surgery be contemplated without prior discussion with the the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call)

22. Decisions over the total length of treatment will depend on the certainty of diagnosis, clinical course, culture results and will need involvement of the orthopaedic and microbiology teams. Treatment of osteomyelitis is usually for a total of 6 weeks, which includes the initial IV course.

23. Liaise with microbiology on choice and duration of oral step-down antibiotics when the patient is well and inflammatory markers are improving. For dosage on oral antibiotics, please see BNFC.

6. EMERGENCY MANAGEMENT- POTENTIALLY LIFE THREATENING CONDITIONS

Please discuss early with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call) for advice and transfer if required.

1. Splenic and Hepatic Sequestration

Acute Splenic Sequestration (More common in young children).

Presentation:

- Sudden onset of tachypnoea, pallor, abdominal pain and splenic enlargement.
- Precipitated by fever, dehydration and hypoxia.
- Rapid sequestration of red cells can lead to a sudden fall in haemoglobin and death from hypoxic cardiac failure with pulmonary oedema.
- May have a more insidious onset.

Investigation:

- FBC + reticulocyte count
- G+S (+red cell phenotype if not previously performed)
- Blood culture
- U&Es, creatinine, LFTs, CRP
- Store serum for virology

Management:

- Assess the need for volume expansion and obtain IV access.
- Crystalloid should be used with caution as this may exacerbate heart failure.
- Organise for phenotypically matched red cell transfusion without delay (if in extremis, use uncrossmatched O negative).
- Broad-spectrum antibiotics to cover *Streptococcus penumoniae* and *Haemophilus influenzae*:- see infections section.
- Patients with recurrent splenic sequestration should be considered for splenectomy after prior administration of Pneumovax, Men C and Hib vaccines.

Hepatic Sequestration

Presentation/Investigation/Management

- Less common than splenic sequestration in children but treated in the same way.

2. Abdominal pain due to Biliary Colic / Sepsis / Girdle syndrome

Presentation/Investigation/Management

- Biliary colic +/- biliary sepsis or girdle syndrome.
- Investigations include U+Es/LFT/amylase/USS abdomen.

- Girdle syndrome presents with severe abdominal pain, abdominal distension, hepatomegaly, reduced bowel sounds, and should be managed as for acute chest syndrome (ACS).
- All biliary complications should be discussed with the paediatric surgical team.
- Manage with IV fluids, IV antibiotics (ceftriaxone +/- metronidazole), analgesia, consider ERCP/MRCP.

3. Acute Chest Syndrome (ACS)

Presentation:

- Caused by sickle cells occluding pulmonary blood vessels.
- Characterised by pleuritic chest pain, fever, abnormal chest examination and new pulmonary infiltrates on the chest X-ray.
- A common cause of death and may be a postoperative complication in older children. Characterised by “T-shirt” distribution of pain, signs of lung consolidation (often bilateral), hypoxia, tachycardia, tachypnoea and pyrexia.
- Coughing is a late symptom.
- Physical signs may precede X-ray changes by up to 12 hours. However chest X-ray changes can also precede signs.
- Falling Hb without evidence of splenic or hepatic sequestration is an indication for chest X-ray. A rapid deterioration requires urgent treatment.
- It is sometimes difficult to tell the difference between ACS and a chest infection, early transfusion is often appropriate and frequently life saving.

Investigations:

- As per routine baseline investigations, in addition:
- HbS%
- Capillary blood gas
- Chest X-ray
- Sputum and blood cultures
- Urine pneumococcal antigen & blood pneumococcal PCR (EDTA bottle)
- Sputum/induced sputum for atypical pneumonia PCR (need to discuss with microbiologist)
- Mycoplasma serology (need to discuss with microbiologist)

Management:

- Most important is prompt recognition of ACS & early discussion with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call).
- IV fluids as in painful crisis (watch carefully for fluid overload and reduce fluids when exchange transfusion is completed).
- Pain management, consider use of PCA early.
- Maintain target oxygenation (>94%) and monitor with pulse oximetry.
- Regular bronchodilators by nebuliser.
- Prevent further atelectasis using incentive spirometry, CPAP and PEEP, chest physiotherapy.
- Early HDU/CICU/anaesthetic referral.

- Ventilatory support may be required.
- Treat underlying infection (Ceftriaxone 80mg/kg plus clarithromycin, see BNFC).
- Transfusion (as discussed below).

Transfusion:

- Decisions regarding transfusion are best guided by patient's clinical condition.
- The purpose of transfusion is to:
  - enhance oxygen-carrying capacity
  - improve tissue oxygen delivery
  - reduce HbS concentration to reduce sickling
  - prevent progression to acute respiratory failure
- Transfusion commonly results in impressive improvement within hours.
- Simple transfusion is indicated for patients with:
  - mild or moderate chest syndrome, particularly with falling Hb levels
  - aim for Hb level of no more than 100g/L
- Exchange transfusions are used to:
  - reduce the Hb S concentration rapidly whilst avoiding the problems associated with increased fluid volume and viscosity
- Exchange transfusion is indicated when there is evidence of:
  - clinical deterioration
  - worsening x ray changes
  - hypoxia (pulse oximetry less than 90%)

4. Pnemococcal and Haemophilus Septicaemia/Meningitis

- Consider Pneumococcal/Haemophilus septicaemia or meningitis in any febrile sickle cell child.
- Treat with IV antibiotics without waiting for culture results as per UHL Sepsis guideline (please see; **Meningitis UHL Childrens Medical Guideline** & **Pneumonia – Community Acquired UHL Childrens Hospital Guideline** for ongoing management).

5. Malaria

- Needs urgent anti-malarial therapy appropriate to the zone of infection.
- Enquire about travel history.
- Management as per **Malaria UHL Childrens Medical Guideline.** If needed contact Hospital for Tropical Diseases (via switchboard) for up-to-date information.
- Transfusion is often necessary as haemoglobin may fall significantly due to increased haemolysis.

6. Aplastic Crisis

Presentation:

- Onset of profound anaemia over 1 – 3 days with reticulocytopenia without sequestration.
- Due to transient marrow hypoplasia commonly induced by parvovirus, but other viruses can be responsible.

Investigation:

- As per routine baseline investigations, in addition:
  - Parvovirus DNA and antibody titres

Management:

- If there is no reticulocyte response or the patient is cardiovascularly compromised, consider transfusion.
- Immunity appears to be lifelong.

7. **Pyrexia associated with chelation therapy**

- Patients on chelation therapy with desferrioxamine presenting with pyrexia and/or diarrhoea/abdominal pain should be treated for Yersinia enterolitica. Stool for Yersinia culture should be organised (specifically state Yersinia culture on request form to ensure correct incubation), treat as per infection section of this policy and discuss all cases with microbiology. Chelation therapy must be stopped.
- Note risk of neutropenic sepsis with deferiprone (agranulocytosis) and deferasirox (cytopenia).

7. ACUTE NEUROLOGICAL COMPLICATIONS (SEE APPENDIX 4)

Please contact the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call) for advice and transfer:

1. These may present as: acute severe headache, transient ischaemic attacks, seizures or arterial ischaemic stroke.

Arterial Ischaemic Stroke

2. 10% of children with sickle cell disease will have a stroke before the age of 20 and 25% of this group will have evidence of ischaemic brain injury on MRI, even if they have been clinically asymptomatic.

Presentation:

3. There is often a significant delay between stroke onset and diagnosis in children, usually because of failure to recognise the significance of the acute clinical presentation. The commonest clinical presentation of childhood arterial ischaemic stroke (AIS) is acute hemiparesis. About 20% of AIS is referable to the posterior circulation and hence clinical signs may include ataxia, vertigo and vomiting. Seizures occur in 20% of children.
4. Acute neurological signs may not be clear cut in a child with AIS due to sickle cell disease, who present more commonly with 'soft signs' and there should be a low threshold to suspect the diagnosis in this group of children.

Any new neurological signs in children with sickle cell disease should be evaluated as potentially being a stroke

Investigations:

1. Brain MRI is recommended for the investigation of children with clinical stroke.
2. Brain MRI should be undertaken as soon as possible after presentation. If brain MRI will not be available within 48hrs, CT is an acceptable initial alternative.
3. Brain imaging should be undertaken urgently in children with clinical stroke who have a depressed level of consciousness at presentation or whose clinical status is deteriorating.
4. Consider transthoracic cardiac echocardiogram within 48 hours after presentation in all children with arterial ischaemic stroke.

Management: ABC

- Blood pressure should be maintained at an adequate level to optimise cerebral perfusion
- Adapted from RCPCH guidelines:

1. All children with stroke should have regular assessment of conscious level and vital signs
2. Urgent exchange transfusion should be undertaken to reduce HbS% to <30% and raise haemoglobin to 100g/l (avoid >110g/l).
3. If the patient has a neurological event in the context of severe anaemia (e.g. splenic sequestration or aplastic crisis), or if exchange transfusion is going to be delayed for more than 4 hours, urgent top-up blood transfusion should be undertaken.

Multidisciplinary assessment: Adapted from RCPCH guidelines

- As soon as possible after admission, all children following stroke should have an evaluation of:
  - swallowing safety
  - feeding and nutrition
  - communication
  - moving and handling requirements
  - position requirements
  - risk of pressure sore assessment
- All children affected by stroke should have a multidisciplinary assessment within 7 days of admission to hospital.

Secondary Prevention

1. Regular blood transfusion (every 3 to 6 weeks) should be undertaken to maintain the HbS% <30% and Hb 100 -110g/l.
2. Transfusion may be stopped after 1 year only in patients who experience stroke in the context of a precipitating illness, e.g. aplastic crisis and whose repeat vascular imaging and Transcranial Doppler velocities are normal at this time.
3. Those who cannot receive blood transfusions because of allo-immunisation, auto-antibody formation or non-compliance with transfusion or chelation should be recommended for treatment with hydroxycarbamide.
4. Addition of aspirin (for dosage see BNFC), neuro-revascularisation procedures and bone marrow transplantation should also be considered.

8. MANAGEMENT OF PRIAPISM

1. A sustained, painful and unwanted erection of the penis. The mean age at which priapism occurs is 12 years, and by the age of 20, as many as 89% of males with SCD will have experienced one or more episodes of priapism.
   a. Stuttering priapism – recurrent episodes that last from minutes up to 3 hours. Pain can be of variable intensity and the penis may not be fully erect. Risk of progressing to prolonged event.
   b. Prolonged priapism – longer than 3 hours. Often very painful with high risk of cavernosal fibrosis and impotence. Must be treated urgently.
2. Typically priapism affects the corpora cavernosae, very rarely the corpus spongiosum may be affected. Penile ischaemia and acidosis begin to occur about 6 hours into a sustained priapic episode.
3. Many patients are not aware that priapism is a complication of sickle disorders and may be reluctant to discuss it. Stuttering priapism is under-diagnosed, symptoms should be specifically asked for at outpatient clinic visits.

4. It is vital to attend for treatment as early as possible. Delay may increase the risk of cavernosal fibrosis and impotence. Discuss patients with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call) & paediatric surgical team out of hours.

Triggers

- fever
- dehydration
- cold exposure
- full bladder
- REM sleep
- alcohol
- sexual arousal

General principles of management of priapism – Home treatment

- Attempt to urinate
- Try warm bath
- Try gentle exercise
- Hydration
- Oral analgesia
- Oral etilefrine if previous episodes of priapism

IF EPISODE OF PRIAPISM LASTS FOR >1 HOUR, PATIENTS & FAMILIES SHOULD BE ADVISED TO ATTEND THE EMERGENCY DEPARTMENT

Acute management of prolonged priapism <u>(also see flow diagram below)</u>

Investigations

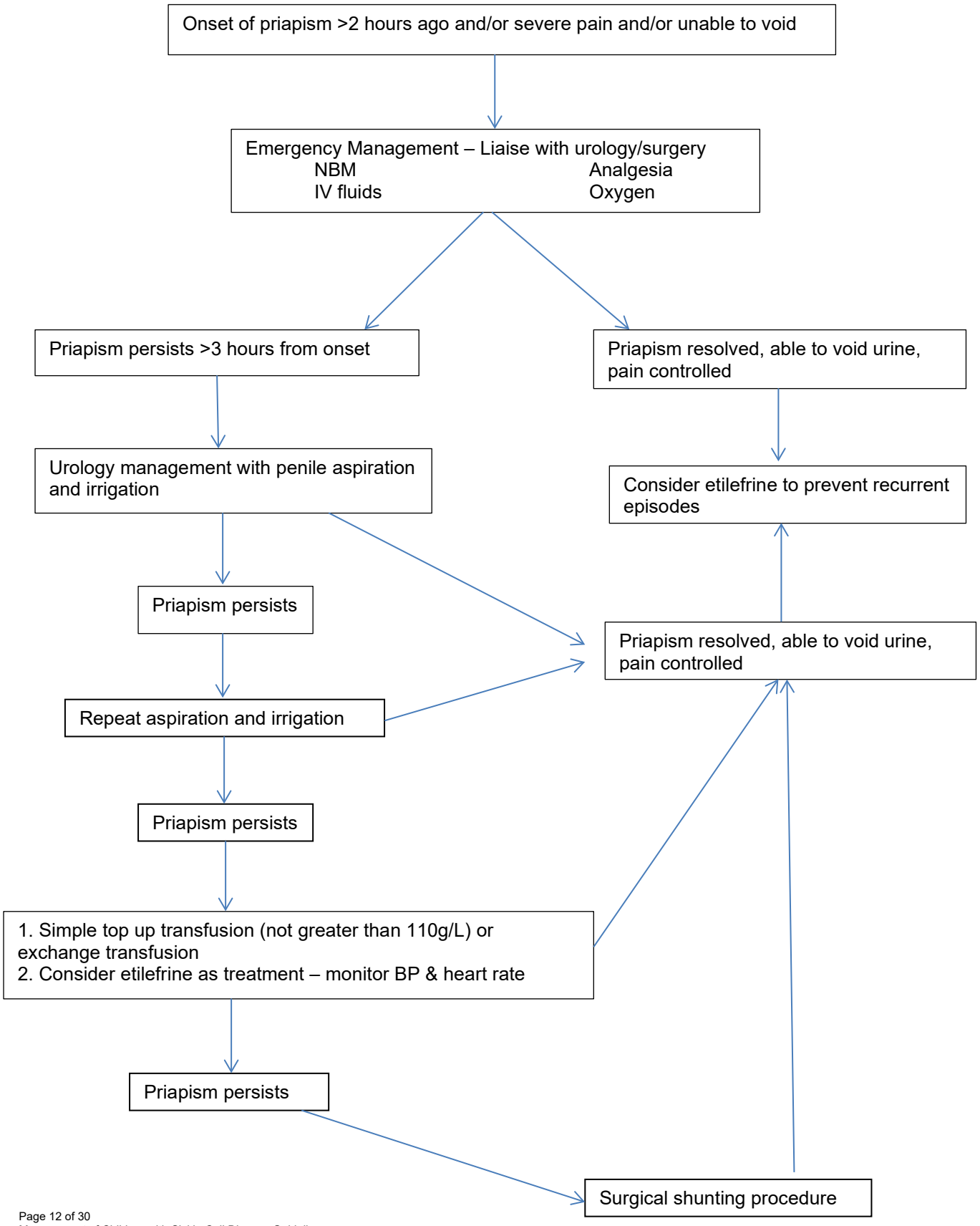
- FBC, reticulocyte count
- Urinalysis +/- culture
- Group and save

Management

- Liaise with paediatric surgical/urological team and the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call)
- Keep NBM in case surgical intervention is needed.
- IV fluid (10ml/kg bolus followed by 100% maintenance).
- Analgesia (careful use of opioids to avoid urinary retention).
- Supplemental oxygen to keep saturation >95%.
- Never use ice packs to manage priapism in patients with sickle cell disease.
- Refer to paediatric urology/sugery if no improvement within 3 hours of onset of symptoms:
    - Urological management involves penile aspiration and irrigation using epinephrine solution.

- This may need to be repeated if detumescence (resolution of erection) does not occur
- Blood pressure and heart rate should be monitored as side effects include hypertension and tachycardia
- If detumescence does not occur despite above supportive measures and repeated aspiration and irrigation - top up transfusion (up to maximum 110g/L) or exchange red cell transfusion should be performed and surgical intervention/shunting may be needed

Acute management of prolonged priapism



Recurrent priapism

- Patients and families should be education about this sickle related complication so that it is not under-recognised. Critically boys and parents must be made aware prolonged priapism is an emergency and untreated can lead to impotence.
- Recurrent episodes can be prevented by using Etilefrine
    - <2 yrs 1-2.5mg PO TDS
    - 2-6yrs 2.5-5mg PO TDS
    - >6yrs 5-10mg PO TDS
    - Should be used with caution in patients with diabetes mellitus, hypercalcaemia, hypokalaemia, severe renal impairment and cor pulmonale.
    - Aim to take with food. Side effects include palpitations, tremor, chest pain, arrhythmias, restlessness, insomnia, sweating, dizziness and gastrointestinal symptoms.
    - Blood pressure needs to be monitored weekly initally then monthly and treatment stopped if above 90th centile for age or expereicening increasing headaches/symptoms suggestive of TIA.

9. PROTEINURIA / HAEMATURIA

Definition

- Early morning albumin/creatinine ratio > 3.0 mg/mmol or > 1+ proteinuria in a dilute urine specimen.
- Nephrotic syndrome: proteinuria ≥ 3+ on dipstick (UA/UC >200mg/mmol), oedema, plasma albumin <25g/l ± hyperlipidaemia.
- Haemastix positive does not necessarily mean there will be proteinuria.

Aetiology

- Transient, orthostatic, glomerulonephritis, nephrotic syndrome, tubulo-interstitial disease

Sickle Cell Nephropathy

- Possibly due to mesangial phagocytosis of sickle cells, an immune complex mediated process, glomerular hypertrophy or glomerular injury by hyperfiltration. Kidneys show focal segmental glomerulosclerosis. May progress to nephrotic syndrome and end stage renal failure.

Investigations:

Urine

- urine albumin/creatinine ratio on first morning urine and pm ambulatory sample
- urine microscopy and culture
- urinalysis for blood and glucose

Blood

- FBC, renal profile

Radiology

- Renal tract ultrasound

Once orthostatic proteinuria has been excluded

- ESR, EMU osmolality
- Autoimmune/vasculitic screen
- DMSA scan

Management:

- Stop NSAIDs, review all medication, monitor BP

When to refer to Nephrology and indications for biopsy

- Duration > 6 months
- Excretion > 1 g/24 hours
- Family history of renal disease
- Macroscopic haematuria
- Sustained hypertension
- Renal failure
- Hypocomplementaemia
- Age less than 1 year or greater than 10 years
- Hypertension, proteinuria, increasingly severe anaemia and haematuria predict renal failure in sickle cell patients

10. BONE AND JOINT PROBLEMS

Osteomyelitis causative organisms:

- *Salmonella species*
- *Staph aureus, Haemophilus influenzae*
- *E-Coli and other Gram -ve bacteria (such as Klebsiella spp)*
- *Enterobacter spp*
- *Mycobacterium spp*

Diagnosis of osteomyelitis:

1. This is very difficult to diagnose in sickle cell disease. Signs and symptoms can be similar to acute pain crisis. Clinical distinction can be difficult especially with the increased use of antibiotics in painful vaso-occlusive crises.

Clinical Features:

2. These usually include: pain, swelling, tenderness. Usually the child is systemically unwell. The commonest sites are the femur, tibia and humerus. Remember that fever may be modest. Presentation could be acute or occur over a period of a few weeks. Suspect osteomyelitis if pain is unusual and does not resolve as expected with analgesia.

Investigations:

- FBC, CRP, aerobic/anaerobic blood cultures
- Stool samples (Salmonella)

- Throat swabs for M,C&S
- NPA for virology if viral infection is suspected
- Bone, pus or tissue samples should be sent to Microbiology for M,C&S, AFB and for 16S rDNA molecular studies.

Radiology:

3. **X-ray:** Early X-rays are of limited value. X-ray changes do not appear until about 10 days after infection and can be similar to that seen in a painful crisis.
4. **Ultrasound:** Rapid, non-invasive and easy to target areas of maximum pain. Changes are non-specific and findings are similar to those seen in acute pain crisis.
5. **MRI:** Useful in monitoring treatment.
6. No single imaging technique can reliably distinguish acute infection from infarction.

Treatment:

7. See under infections section.
8. Under no circumstances must surgery be contemplated without prior discussion with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call). The patient will require blood transfusion prior to general anaesthetic if surgery required– see policy for general anaesthesia.

Avascular Necrosis of the Shoulders and Hips

9. This complication should be suspected particularly in older children with persistent pain affecting the hip, shoulder, knee, leg or groin. Pain may be worse on movement though also occurs at rest. Often there is restriction of movement at the hip and shoulder joint.

Diagnosis:

10. An x-ray should be considered in those patients with persistent/prolonged or recurrent pain.
11. MRI may help with diagnosis.

Management:

12. Analgesia, adequate rest, avoidance of prolonged weight bearing.
13. Refer for physiotherapy and consider hydrotherapy.
14. Programme of gradual non weight bearing exercise – particularly swimming, cycling.
15. All cases should be discussed and referred for orthopaedic assessment.
16. Consider review of hydroxycarbamide therapy if thought to be precipitated/exacerbated by this.
17. Consider transfusion programme in those requiring surgery, debilitated by pain or restricted movement as may prevent progression of damage. Review transfusion programme at 6 monthly intervals.

11. EYE PROBLEMS

1. Patients should be made aware of sickle cell related eye complications. Routine ophthalmological screening is not indicated, however community opticians review should be encouraged. Patients/parents should be advised to report changes in visual acuity, altered/distorted vision, presence of floaters as a matter of urgency and referral made to paediatric ophthalmology clinic for assessment.

2. All patients on iron chelation therapy should have annual screening for chelation associated cataract/retinopathy formation.

12. TRANSFUSION IN SICKLE CELL DISORDERS

1. See Haemoglobinopathy transfusion UHL childrens hospital guideline

   http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Haemoglobinopathy%20Transfusion%20UHL%20Childrens%20Hospital%20Guideline.pdf

2. Anaemia alone in an otherwise well child is not an indication for transfusion unless Hb falls to 5g/dl or lower, in which case discuss with the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call) with details of previous results. Check reticulocyte counts. Use Kell compatible, Rhesus compatible blood matched for antibody status.

Simple or 'top-up' transfusion:

3. Indicated for acute anaemia e.g. aplastic, sequestration crisis or acute bleeding. To calculate volume of packed cells required use trust guidance.

Note:

- Do not transfuse to above 110g/l.
- The volume transfused should be capped at 3 units for children >50kg.
- Document indication for transfusion clearly in notes.

Chronic transfusion programme in day unit setting:

4. **Definition:** Repeated transfusions to keep Hb S <30% over a period of time.
5. Transfuse at 3 to 4 week intervals to suppress erythropoiesis and keep Hb S <30%. Aim for Hb no more than 11g/dl.
6. Patients vary in the frequency and amount of blood required to suppress HbS production. In children with SC disease it is usually necessary to start with an exchange transfusion. In other children with HbSS (particularly those with a high initial haemoglobin level) exchange may be necessary at times.

Prior to commencing transfusion programme potential complications of transfusion must be discussed and documented.

- Transfusional iron overload.
- Transfusion transmitted infection – aim for Hepatitis B/C + HIV screen prior to starting.
- Transfusion reactions.
- Antibody formation.
- Ensure hepatitis B vaccination status satisfactory.

Monitor:

- Hb, Hb S%, red cell alloantibodies monthly.
- Serum ferritin every 3 months.
- Start iron chelation when serum ferritin is 1000ug/L or after 10 transfusions.

- Annual viral screen (HIV, hepatitis B & C) + check immunity to Hep B vaccination –anti-Hep B surface antibody.

13. POLICY FOR GENERAL ANAESTHESIA

1. All children with sickle cell disease should be discussed with the paediatric haemoglobinopathy and anaesthetic team when they are booked for surgery so that a coordinated plan can be made for their care.
2. These patients should be scheduled early on the operating list to avoid prolonged fasting time.
3. Care should be taken to avoid factors which may precipitate the development of a crisis. These include hypoxia, dehydration, acidosis, cold and pain. The majority of crises in the operative period occur postoperatively.
4. All patients should have at least 2 hours of IV hydration if surgery is delayed and should continue postoperatively until oral fluids are tolerated.
5. All patients with HbSS and HbS/beta thalassemia should receive a blood transfusion prior to the procedure to reduce the risk of perioperative complications up to a haemoglobin no higher than 110g/l.
6. A preoperative blood transfusions will be organised by the paediatric haemoglobinopathy team.
    - A HbS % is not necessary pre surgery unless exchange transfusion is required (see below).

Transfusion Recommendation for Elective Surgery:

7. The TAPS study showed that preoperative transfusion was associated with decreased perioperative complications and therefore suggested that all patients should be considered for preoperative transfusion (including low-risk and medium risk surgeries as below).

    1. **Low risk surgery** short procedures with minimal risk of perioperative complications, e.g. grommets or GA for scans in children who have no other risk factors:
        - **Hb should be ≥ 70g/l and below 100g/l**

    2. **Medium risk surgery:** tonsillectomy, splenectomy, laparoscopic cholecystectomy, hip/knee replacements. History of obstructive sleep apnoea. Children with a history of recurrent chest problems or other chronic health problems:
        - **Simple transfusion to an Hb of 100g/l, regardless of HbS levels**

    3. **High-risk surgery:** thoracic, major upper abdominal surgery or neurosurgery and children with a history of severe sickle related problems e.g. previous CVA. Consider in eye surgery, surgery involving tourniquets:
        - **Transfuse or exchange transfuse to reduce the HbS level to <30%**
        - **Total Hb should not be > 110g/l**

8. Children with sickle cell disease may be difficult to exchange transfuse and will require early consultation. Exchange transfusion is difficult to perform, particularly in small children and should not be carried out unless absolutely necessary.
9. Children and their parents should be involved in the decision to transfuse whenever possible.
10. Children requiring emergency surgery should be treated similarly if time allows. If this is not possible, blood should be cross-matched and standing by in case of perioperative problems requiring emergency exchange transfusion.
11. All patients must be discussed with the paediatric haemoglobinopathy clinical team at presentation.

14. COMMON SURGICAL PROCEDURES

Adenotonsillectomy

1. This is normally indicated for children with tonsillar/adenoidal hypertrophy and confirmed obstructive sleep apoea (OSA) demonstrated on sleep study.
2. The input of the ENT team and respiratory teams will be required when planning for this procedure.
3. Children with severe OSA and/or additional risk factors (eg cerebrovascular disease, chronic lung disease etc) should also be discussed with intensive care for management prior to the procedure.

Laparoscopic cholecystectomy

4. This is indicated for children with recurrent biliary colic/cholecystitis.
5. A thromboprophylaxis risk assessment should be carried out and treatment instituted as appropriate.

Splenectomy

6. This is normally indicated for children with recurrent splenic sequestration (>2 episodes requiring transfusion therapy or 1 life threatening episode) or chronic hypersplenism. Cholecystectomy could be considered at the same time for those children with additional recurrent biliary colic/cholecystitis.
7. A thromboprophylaxis risk assessment should be carried out and treatment instituted as appropriate.
8. If not previously vaccinated, 1 month prior to scheduled splenectomy, the patient should receive pneumococcal, HiB conjugate, Men C conjugate and 5 yearly pneumococcal vaccination.
9. Thrombocytosis is common post splenectomy. For sustained platelet counts >1000x10^9 discuss with paediatric haematology team.

15. HYDROXYCARBAMIDE

Hydroxycarbamide has been shown in a large randomised-controlled study to decrease the frequency of painful vaso-occlusive crises and chest crises in adults with homozygous sickle cell disease. There is accumulating experience of its use in children and a significant benefit in survival has been demonstrated in those given hydroxycarbamide.

1. Hydroxycarbamide is an S phase-specific cytotoxic agent, which has been used for many years to treat myeloproliferative conditions. It has also been used to treat children with secondary polycythaemia. Its side effects include bone marrow suppression, gastro-intestinal disturbances and increased skin and nail pigmentation. There is no available evidence that hydroxycarbamide affects fertility. It is potentially teratogenic as high doses are teratogenic in animals, though effects in humans are unknown.

2. The mechanism of action is not certain. Three effects may be important:

   - Increase in fetal haemoglobin content within the red cell, inhibiting sickle haemoglobin polymerisation.
   - Decreased adhesion molecule expression on the surface of the red blood cell, reducing red cell-endothelial adhesion.
   - Reduction of white cell and platelet count. This may also impair the sickle cell/endothelial interaction and reduce inflammatory process in the microvasculature.

Indications for use

- Offer to all patients with homozygous sickle cell disease and sickle beta thalassaemia, as has shown significant benefit in survival.

Previous indications remain if patients not on hydroxycarbamide:
- Recurrent painful crises, significantly interfering with lifestyle. In practice, this would be more than three hospital admissions with painful vaso-occlusive crises per year.
- Recurrent chest crises, two or more a year.
- Avascular necrosis.
- Recommend in those children with high risk transcranial Doppler velocities where transfusions are not possible.
- Treat patients with conditional velocities to help prevent progression to abnormal TCD velocity.
- Patients who have started regular blood transfusions for abnormal TCD velocity can be switched to hydroxycarbamide therapy if they have received at least 1 year of transfusions and have no vasculopathy on MRI.

Exclusions

- Anaemia with Hb <60g/l at baseline.
- Platelets $<100x10^9$/l, neutrophil count $<1x10^9$/l, reticulocytes $<80x10^9$/l.
- Decompensated cardiac, renal, liver or pulmonary disease.

Procedure Prior to Starting Therapy

3. The benefits and hazards of using hydroxycarbamide should be considered for each individual patient, and discussed with the patient and parents. Give detailed explanation of treatment, including nature of possible side effects and a copy of the Patient Information Leaflet. Where appropriate, discussion about the risks of becoming pregnant or fathering a child while on hydroxycarbamide should occur.

4. Sperm banking should be considered in older male adolescents.

5. Contraception is advised.

6. Ensure that the patient is willing to attend regularly to monitor effect.

Baseline investigations

- Height and weight centile. Tanner stage
- FBC, reticulocytes
- Renal, liver, bone profile

Dosage

- Start at 20mg/kg, as a single dose.
- Increase dose by 5mg/kg every 8-12 weeks to maximum tolerated dose (up to 35mg/kg/day).
- Ideally aim for dose that controls symptoms while maintaining neutrophils $>1 \times 10^9$/L.
- Continue regular penicillin V and folic acid.

Monitoring of Therapy

FBC and reticulocyte count should be checked 2 weeks after commencement and after every dose increment.
Then monitor every 8-12 weeks for the entirety of treatment.

Three-monthly: clinical assessment: frequency of crises, other adverse sickle events, height and weight centile, Tanner stage, toxicity recording, compliance monitoring

Dosage Modification

- If neutrophils <1 x10^9 /L, platelets <80 x10^9 /L, reticulocyte <80 or 20% decrease in Hb below baseline - stop medication.
- Recheck FBC weekly.
- When counts back to normal, restart at same dose if transient or reduce by 5mg/kg and continue to check FBC after 2 weeks.
- Continue during admission unless febrile neutropenia or bleeding with thrombocytopenia.

Assessment

7. Assess clinical response, Hb F% and adverse events at 3 and 6 months.

8. 6 months on maximum tolerated dose required prior to considering discontinuation.

16. CRIZANLIZUMAB

- Crizanlizumab is a humanised monoclonal antibody that binds to P-selectin and blocks the interaction between red cells, endothelial cells, leucocytes and platelets, preventing vaso-occlusion.

- It has been approved by NICE for young people aged 16 years and over who suffer with recurrent painful chest crisis.

- It is administered intravenously but prior agreement is requried through the regional haemoglobinopathy MDT.

17. OUTPATIENT MANAGEMENT

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 disease.

New Patients

- Usually referred following neonatal screening, but also patients presenting from overseas/moved into area.

Registration:

1. FBC, RETICULOCYTE
2. Haemoglobinopathy screen (sickle solubility test, Hb electrophoresis, Hb A_2 and F estimation by HPLC), G6PD screen
3. Blood group, red cell phenotype
4. Take full family history including names, ages and plans for future children.
5. Explain to parents the probable diagnosis and its implications, including genetic counselling.
6. Issue haemoglobinopathy card and demonstrate splenic palpation to parents of young children.
7. Measure height and weight and document on growth chart, pulse oximetry, BP.
8. Faltering growth should be managed with the nutrition team and nutritional intervention considered.

9. Document any sickle-related or other illness since last visit, immunisation status, school progress and attendance and holiday plans. Ask about bed-wetting, priapism (boys). Sleep study should be organised for signs and symptoms of upper airways obstruction.
10. Enquire about learning/behavioural concerns, discuss at psychosocial MDT if identified. Healthy lifestyle advice should be given.
11. Ensure regular supply of penicillin V, folic acid provided by GP. Discuss use of analgesics and ensure GP prescribes supply.

Arrange follow up:

- 3 monthly until age 12 months.
- 4 – 6 monthly ages 1-3 years.
- 6 monthly thereafter, unless clinical indication for earlier review.
- 12 monthly for children with Hb SC disease if clinically stable.

Screening investigations

12. Transcranial doppler screening (TCD) should be organised for all children with homozygous sickle cell disease or HbS/thalassaemia over the age of 2 at least annually (more frequently depending on results – see National TCD screening protocol).
13. Screening for pulmonary hypertension should occur 5 yearly from age 15 with echocardiogram (request TR jet velocity). An echocardiogram might be required earlier than this for investigation of hypertension, unexpected heart murmur, disproportionate cardiomegaly or on the advice of the cardiologist. Screening for chronic sickle lung disease should be organised 5 yearly from age 15. Those patients with recurrent acute chest syndrome should be referred for respiratory input.
14. Screening for sickle nephropathy should be organised annually with urinalysis from age 15 and urine protein creatinine ratio (UPCR) organised for those with significant proteinuria. See table below for other screening investigations.

Communication with patient / MDT

15. Copies of correspondence should be sent to patient, GP and community services. This should have contact details of the paediatric haemoglobinopathy team. A patient information sheet detailing services provided and list of contacts should be made available to new patients. Patient information should be made available covering discussion in clinic e.g. TCD, hydroxycarbamide.

Annual review

16. This should be done by a member of the haemoglobinopathy team.
17. It should include review and documentation of acute episodes and complications over the previous year, current medication, transfusion parameters, iron monitoring and iron chelation therapy for those on regular transfusion.
18. Checking to ensure that routine screening investigations and vaccinations are up to date.
19. Discussion of disease-related issues relevant to the patient and family.
20. If appropriate, a discussion of treatment options including hydroxycarbamide, transfusion and bone marrow transplantation.
21. Routine investigations at annual review are shown in the accompanying table.

Policy for children not brought to clinic (WNB)

22. Patients who WNB on 3 consecutive occasions or young infants on the first appointment should be followed up by the nursing team and a letter sent to GP and patient. Referral of children who move to

another region should be organised by the specialist centre and community teams to ensure appropriate community input.

18. PREVENTION OF INFECTION IN CHILDREN

1. Antibiotic prophylaxis for prevention of pneumococcal disease is mandatory.

2. **ALL** children with sickle cell disease (including HbSS, HbSC, HbS/Beta thalassaemia) are prescribed Penicillin V by the age of 3 months.

Dosage:

- Birth to 1 year — 62.5mg phenoxymethylpenicillin suspension BD
- 1 to 4 years — 125 mg phenoxymethylpenicillin suspension BD
- > 5 years — 250 mg phenoxymethylpenicillin suspension/tablets BD

Try to get children taking tablets as soon as possible (crushed and mixed with some fruit juice). Pharmacies may be prepared to dispense dry suspension, or to receive a batch of request prescriptions to avoid collecting a repeat prescription for the suspension every week.

For those children who are genuinely allergic to Penicillin, Erythromycin is prescribed instead.

Dosage:

- < 2 years — 125 mg Erythromycin BD
- 2-7 years — 250 mg Erythromycin BD
- > 8 years — 500 mg Erythromycin BD

All subsequent prescriptions should be given by GP.

3. All patients with sickle cell disease require extra immunisations in addition to the routine childhood immunisations as they have asplenia or dysfunctional spleens.
4. The immunisation schedule for these patients should follow the Green Book NHS guidance box 7.1 “Practical schedule for immunising individuals with asplenia, splenic dysfunction or complement disorders”: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/857279/Greenbook_chapter_7_Immunsing_immunosupressed.pdf

Pneumococcal immunisation:

- Particular focus should be given to the pneumococcal schedule for children and young people with sickle cell disease. As well as scheduled pneumococcal immunisations during early childhood, regular boosters are required thereafter.
- This should be specifically reviewed in the patient’s annual review appointment alongside current immunisation recommendations as per the Green Book.

Additional childhood immunisations:

- Follow Green book NHS guidance Box 7.1
- This gives details for vaccination of all patients and includes patients not previously vaccinated.

Influenza vaccine:

- Should be given every year in October/November. To be given by GP.

Malaria prevention:

- Children with sickle cell disease are at increased risk of severe malaria if travelling to endemic areas.
- Many children visit West Africa. Parasite resistance to standard prophylaxis is common and specific advice is especially important. GP to supervise prophylaxis.
- Regimes vary depending on destination and resistance patterns, hence it is imprtant to review up to date guidance. Guidelines for malaria prevention in travellers from the UK: 2022 (publishing.service.gov.uk)
- Chemoprophylaxis should be started before travel and be continued after return. G6PD status should be checked before starting.

Hepatitis B vaccination:

- All non immune children with sickle cell disease should be vaccinated against Hepatitis B. Ideally this should start at 12 months of age. Those children not born in the UK should be vaccinated at the earliest opportunity.
- Vaccination to be three injections at 0, 1 and 6 months (to be given by GP service).
- Vaccinations are recorded in the hospital records and the Child Health Records Booklet.

19.BONE MARROW TRANSPLANTATION

1. Bone marrow transplantation should be discussed as a curative intervention for all patients.
2. Tissue typing of patients, parents and siblings should be carried out if clinical indication for transplantation.
3. Bone marrow transplantation could be considered for patients on sickle modifying intervention:
   - for primary or secondary stroke prevention
   - recurrent acute chest syndrome
   - avascular necrosis
   - recurrent severe acute pain / chronic pain
   - considered for parental preference
4. A thorough discussion and explanation of BMT procedure, benefits and risks should be offered to parents of children with a clinical indication for BMT and histocompatibility testing of siblings organised.
5. If there is willingness to proceed, the child and family should be formally referred to Birmingham Childrens Hospital, giving summary of medical condition, relevant investigations, and a copy of the HLA typing results.

20. ADOLESCENT TRANSITION

- Please see Transitional care UHL policy

  http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Transitional%20Care%20UHL%20Policy.pdf

21. REFERRAL BETWEEN ORGANISATIONS

- All encounters with the patient including in-patient admissions, daycase attendance for transfusion, out-patient clinics and annual reviews are documented by electronic letter.
- Copies of these electronic letters should be sent on to the patient/parents and be made available when referring between organisation.

22. EDUCATION AND TRAINING

Regular teaching provided in ED, Paediatric Specialist Trainees Regional Training days and nursing training programmes.

23. MONITORING AND AUDIT CRITERIA

Key Performance Indicator	Method of Assessment	Frequency	Lead
100% adherence to NICE: Sickle cell acute painful episode - Management of an acute painful sickle guidance (2012)	Retrospective audit	Annual	Paediatric Trust Lead for Haemoglobinopathy

24. SUPPORTING REFERENCES

- National Haemoglobinopathy Peer Review Standards 2014
- NICE: sickle cell acute pain episode: management of an acute painful sickle cell episode in hospital (2012)
- NHS Sickle Cell and Thalassaemia Screening Programme - Standards for the Care of Children with SCD 2010
- Caring for people with Sickle cell and thalassaemia syndromes: RCN competencies: a framework for nursing staff (2011)
- A sickle cell crisis? A report of the National Confidential Enquiry into Patient Outcomes and Death (2008)
- Transition: improving the transition of young people with long term conditions (2006)
- Transcranial Doppler Scanning for Children with Sickle Cell Disease Standards & Guidance: Second Edition (2016)
- Guidelines for the use of hydroxycarbamide in children and adults with sickle cell disease. British Society of Haematology Guideline (2018)
- Sickle Cell Disease in Childhood: Standards and Recommendations for Clinical Care 2019

25. KEY WORDS

Acute chest syndrome, Pain, Sickle cell, Stroke, Transfusion

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.

As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Dr Kaljit Bhuller – Consultant	**Executive Lead** **Chief Nurse**
Details of Changes made during review: • Change from contact Lead Consultant to the paediatric haemoglobinopathy team (if unavailable/out of hours contact the adult haematology team on call) • Inclusion of crizanlizumab as additional therapy	

APPENDIX 1: ANNUAL INVESTIGATIONS TABLE

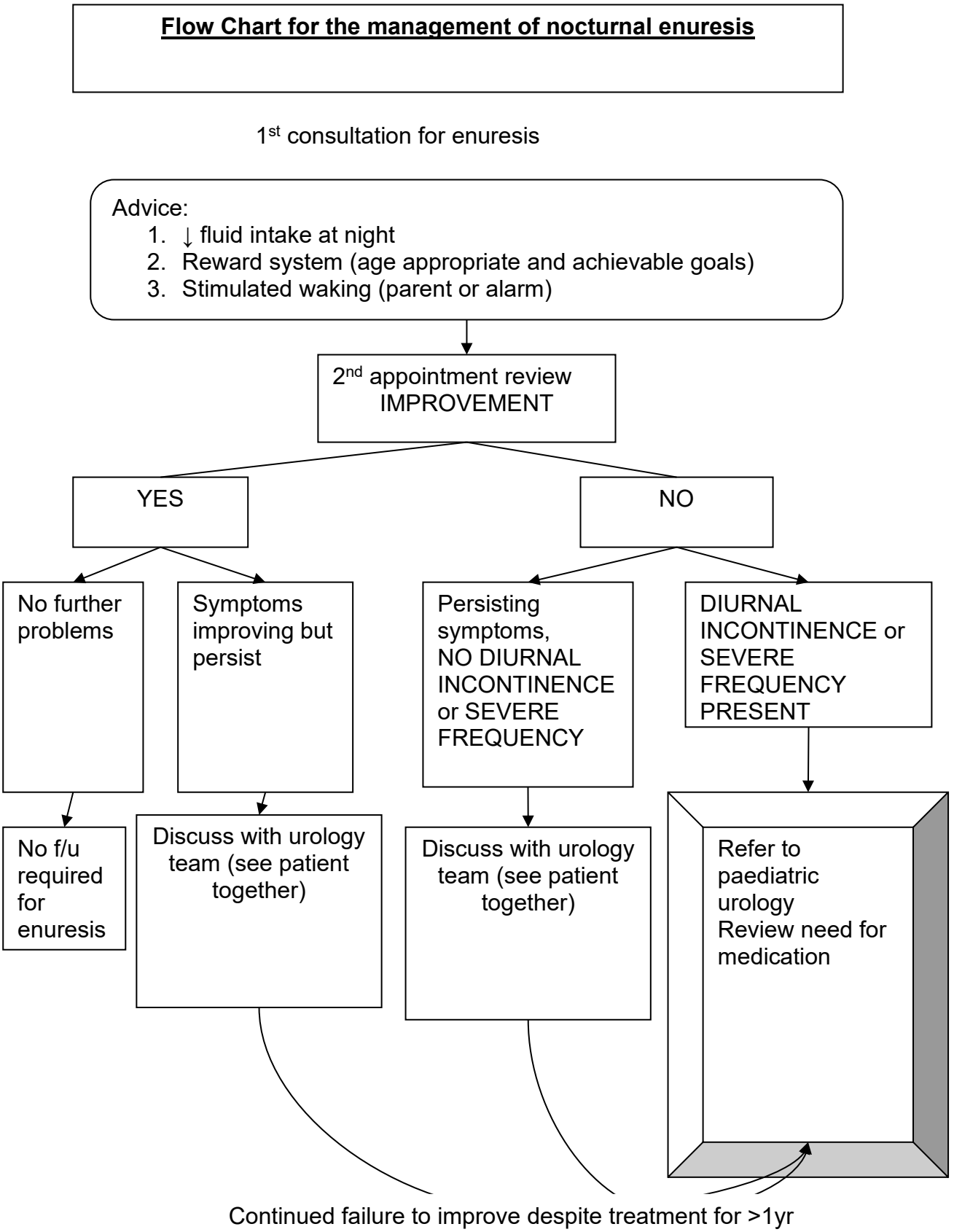
INVESTIGATION OR INTERVENTION	1st APPT	1YR	2YRS	3YRS	4YRS	5YRS	6YRS	7-11YR ANNUAL	12YRS	13YRS	14YRS	15YRS	16-19YRS
FBC/Retics/Biochem/LDH	●	●	●	●	●	●	●	●	●	●	●	●	●
HbF Level		●											
G6PD Level	●												
Blood group full red cell phenotype	●												
HepB Sag, HepC Ab		●											
Transcranial dopplers			●	●	●	●	●	●	●	●	●	●	●
Urine Prot/Creat ratio												●	
Pulmonary function tests / ECHO / R Heart pressure / TR jet velocity												●	

Immunisation*

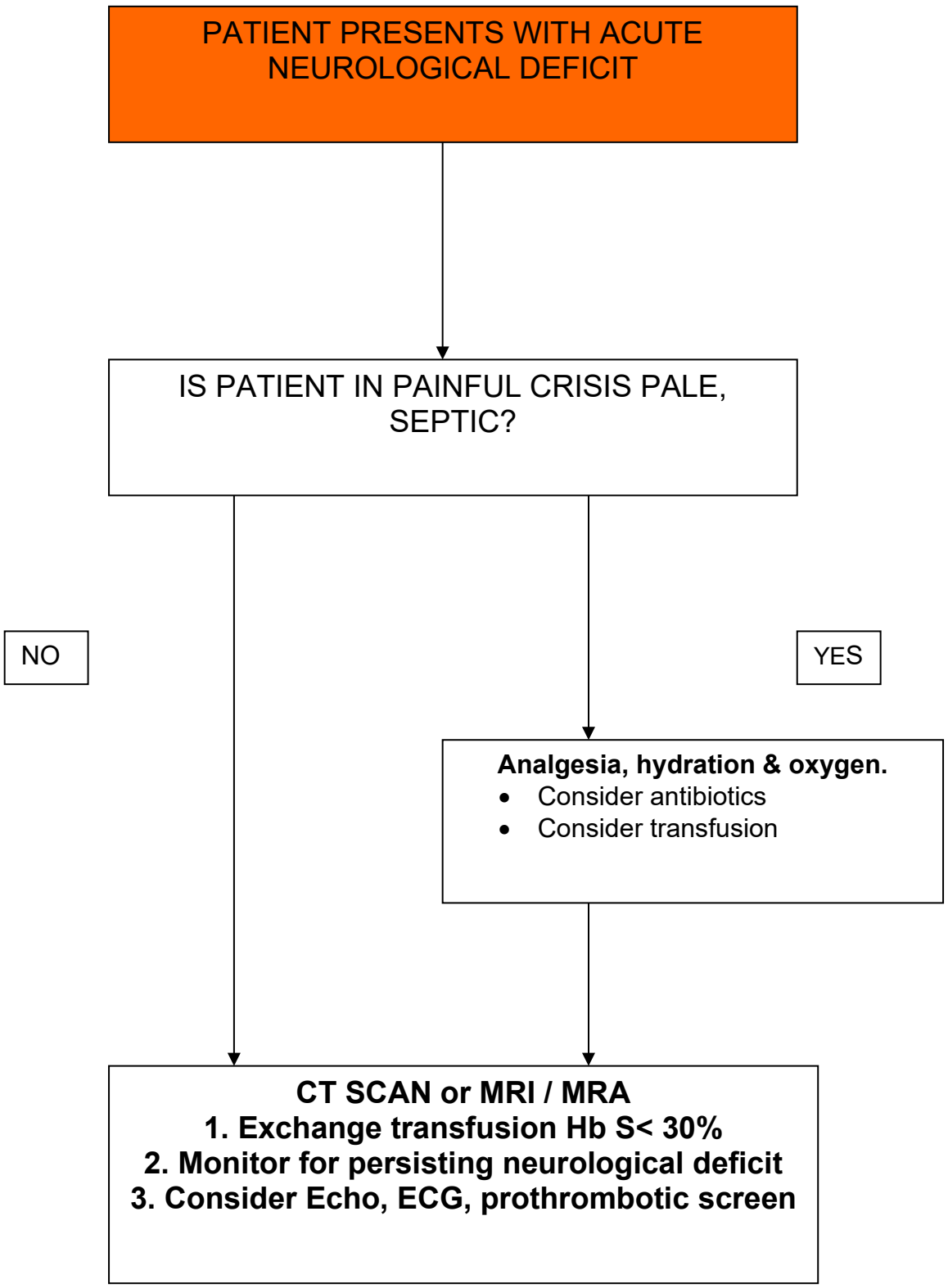
Prevenar (PCV13)	●	●											
Pneumovax (PPV23) (give age 2 & 5 yrly)			●					● Age 7	●				●
Hepatitis B		● Full course											

*Please refer to Green book Chapter 7 immunisation for hyosplenia regarding other additional immunisations

APPENDIX 2: MANAGEMENT OF NOCTURNAL ENURESIS



APPENDIX 3: ACUTE NEUROLOGICAL DEFICIT



University Hospitals of Leicester NHS
NHS Trust

Paediatric Acute Sickle Pain

Assessed by paediatric staff
Medication prescribed by paediatric staff

Child attends with sickle pain
Start protocol if Paracetamol, Ibuprofen, and Codeine Phosphate already given

1st Dose
- Intranasal Fentanyl 1.5 micrograms/kg (max 90 micrograms) single dose

AND
- Morphine Sulphate 10mg/5ml liquid (Oramorph) 300 micrograms/kg (max 10mg)

First doses of analgesia should be given within 15 minutes of presentation
In children < 6 months – refer to BNFC for morphine dosage

Prescribe:
- Regular **Paracetamol** 15mg/kg 6 hourly (8 hourly if under 3 months)
- Regular **Ibuprofen*** 10mg/kg 6 hourly (If over 12 years can have 400mg)

After 30-60 minutes

Assessed by admitting team

2nd Dose
Morphine Sulphate 10mg/5ml liquid 300micrograms/kg (maximum 10mg) given unless respiratory depression/pain free

Pain not improving

Morphine PCA (with background)
See Trust PCA guidelines

After further 60 minutes Pain improving

3rd Dose
Morphine Sulphate 10mg/5ml liquid. 300micrograms/kg (max 10mg)

Pain not improving

Morphine PCA (with background)
See Trust PCA guidelines

Pain improving

Continue **Morphine Sulphate 10mg/5ml liquid**
300micrograms/kg (maximum 10mg) PRN 3 hourly

Observations, Pain Assessment

- Hourly observations for first 6 hours, 2 hourly thereafter
- Paediatric pain specialist nurse (bleep 4101) & Haemoglobinopathy team (X 17801) should review patients daily.
- In general, patients should not be discharged on MST or Morphine Sulphate

Other Medication

The following should be routinely prescribed (refer to BNFc for dosage)

- Constipation: Lactulose/movicol regularly
- Nausea: Ondansetron 100 micrograms/kg 8 hrly PRN (max 4mg/dose) intravenous
- Reversal of opiate induced respiratory depression: Naloxone 4micrograms/kg (initial dose) for partial reversal and repeat after 1 minute if required (cumulative dose no greater than 2mg). If inadequate effect or complete reversal required use 100 micrograms/kg instead, repeated as necessary, to total no greater than 2mg.
- Pruritis: Chlorpheniramine

Alternative to Ibuprofen: Diclofenac (over 6 months only) **Contraindicated in under 1 month*