

Guidelines for In-patient Management of Children with Sickle Cell Disease

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INTRODUCTION:

Sickle cell disease is a relatively common disorder in many parts of the world, including many cities in North America. In many treatment centres, sickle cell disease accounts for a notable proportion of visits to emergency departments and admissions to General Paediatric and Haematology wards. Patients with sickle cell disease are at risk for complications, which can generally be ascribed to their underlying hemolytic anaemia (aplastic crises, gallstones, need for transfusions often in the setting of surgery) or to their sickling or vaso-occlusive state (recurrent painful crises, acute chest syndrome, stroke, priapism, and infections). Infections are related to underlying hyposplenism from vaso-occlusive disease of the spleen. Each of these complications can be very difficult to diagnose and manage. Management is further complicated by the multiple services and physicians involved, often with no consistent approach. This can cause frustration to patients and their families, as well as to health care providers.

In an effort to improve the management of sickle cell patients at The Hospital for Sick Children, we have developed Emergency Department and In-patient guidelines for the management of children with sickle cell syndromes, based on the best evidence available. We also sought the advice of other sickle cell centres in North America (Oakland, Denver, Dallas, Houston, and Miami) and various experts at The Hospital for Sick Children (see Acknowledgments).

In preparing this set of protocols, we have emphasized the interactions among the various services involved in the management of these patients. We have highlighted the specific roles of the key services involved: the Haematology consult service, the Haematology/Oncology on-call service, the Sickle Cell Team (SCT), General Paediatrics, the Emergency Department (ED), and the Critical Care Unit (CCU). Although we have tried to be thorough and comprehensive, due to the multitude of complications that patients with sickle cell disease may encounter, we have not addressed every possible clinical scenario (eg: osteomyelitis {for this refer to the 2004-2005 SickKids formulary p. 286}) but instead we focused on the most common clinical issues encountered in these patients.

We hope that these protocols will be of value in the management of this group of patients. Note that these protocols are intended for the management of patients with sickle cell disease who are sufficiently unwell to present to the Emergency Department and/or be admitted.

TERMINOLOGY

See the Glossary of Abbreviations, near the end of this document, for short forms that are unfamiliar. In addition a number of recurring terms are used extensively throughout these guidelines. These are discussed below.

Haematology consult service refers, during working hours, to the Haematology consult fellow (available from 08h00 to 17h00, Monday to Friday). After working hours, the term refers to the Haematology/Oncology fellow on-call (after 17h00 weekdays and on Saturday, Sunday, and holidays). Although the Division of Haematology/Oncology is a single unit, because of patient numbers Division services are divided into two: the Haematology consult service and the Oncology consult service. Outside of routine working hours, on weekends, and on holidays, however, a combined Haematology/Oncology service is on-call.

Sickle cell disease refers to all clinically relevant homozygous or doubly heterozygous sickle haemoglobinopathies (HbSS, HbSC, HbS β^0 thalassemia, etc.).

Sickle cell anaemia refers specifically to the homozygous disorder, HbSS.

Definitions of **mild to moderate pain** can be found in Appendix 1, where they accompany descriptions of the Oucher test and the Verbal Report Scale.

Seriously ill patients are defined as those:

- in shock
- with sepsis, meningitis, stroke, aplastic crisis, or acute splenic sequestration crisis
- that are decompensating (eg: progressing into chest crisis)
- with O₂ saturation <90% while breathing room air

Acute Painful Episodes (Vaso-Occlusive Crises) Guidelines for Management in Children with Sickle Cell Disease

Background

The cause of vaso-occlusive crisis (VOC) is believed to be ischemic tissue injury from the obstruction of blood flow by sickled erythrocytes. Reduced blood flow causes hypoxia and acidosis. This further increases the sickling process, leading to further hypoxia and acidosis—a downhill spiral that eventually leads to ischemic tissue injury. VOC varies in intensity and duration, both between patients and within the same patient between different episodes. Infection, fever, acidosis, hypoxia, dehydration, sleep apnea, and exposure to extremes of heat and cold can precipitate crises. Often, no cause is identified.

Clinical/Laboratory Features

Painful VOC is the most frequent complication of sickle cell disease. Common sites of pain include bone (extremities, dactylitis or hand/foot syndrome, back) and abdominal pain. Bone pain, the most common type of VOC, may or may not be accompanied by swelling, low-grade fever, redness, and warmth. It may be symmetrical, asymmetrical, or migratory. Dactylitis is a common presentation in infants and toddlers; back and abdominal pain are more common in older children. Abdominal pain in children with sickle cell disease is usually a simple VOC, but other diagnoses may present similarly (splenic sequestration, liver sequestration, appendicitis, pancreatitis, cholecystitis, urinary tract infection, pelvic inflammatory disease, etc.) and should be ruled out. In addition, pneumonia and chest crisis may present as, or accompany, abdominal pain. During a severe painful crisis, a patient may also develop an acute chest syndrome, or a CNS event.

Pain should be treated as early as possible, as persistent pain can debilitate the patient both physically and psychologically. No laboratory features are pathognomonic of VOC; diagnosis is based strictly on the history and physical examination. When treating a painful crisis, the physician needs to be aware that concurrent illnesses such as an acute sequestration crisis, priapism, aplastic crisis, or fever/sepsis (see other protocols) may also occur, which must be dealt with concurrently.

Emergency Department Treatment

Patients present to ED in various degrees of distress.

1. Place patients with concurrent fever of $\geq 38.5^{\circ}\text{C}$ (oral) immediately into a room, and follow the Fever protocol. After antibiotics have been administered, assess the patient thoroughly.
2. Place children without fever in a room as soon as possible, and conduct a brief history and physical concurrently with other measures.
History: nature, duration, location, and severity of pain; how pain compares to previous crises; analgesics already used; associated symptoms.
Physical: vital signs, cardiopulmonary and hydration status, spleen size, neurologic exam, presence of jaundice, and localizing signs of infection.

3. Tests: Request blood counts (CBC, differential, and reticulocyte count.) Consider blood typing and cross-matching if the child is in severe pain, the haemoglobin is 15g/L or more below baseline and reticulocyte count is suggestive of bone marrow suppression. If clinically indicated request urinalysis. If abdominal pain is present and there are clinical indications, may request LFTs +/- amylase. In the presence of chest pain, fever or respiratory symptoms, request a chest x-ray and measure the child's O₂ saturation. {Based on the work by Kress et al (Chest. 1999;115:1316-20)}, pulse oximetry more closely follows co-oximetry than does calculated oxygen saturations reported with arterial blood gases, during sickle chest syndrome.} If there are clinical indications of respiratory failure, arterial blood gases can be measured to monitor pCO₂ levels.
4. Insert an IV if the patient is febrile, dehydrated, or in moderate to severe pain.
5. For fever, acute chest crisis, etc., see other critical pathways (protocols).
6. Give patients assessed to be in mild to moderate pain (see Appendix 1) acetaminophen (15mg/kg/dose) with codeine (1mg/kg/dose) po q4h prn (acetaminophen max. 75mg/kg/day, and codeine max. 60mg/dose and 6mg/kg/day). These can be given separately, or together. Ibuprofen may be helpful (6 mos-12 yrs, 5-10mg/kg/dose po q6-8h, max. 40mg/kg/day or 2400mg/d). Encourage patients to drink. If within 30–60 minutes, pain relief is inadequate, follow guidelines for moderate to severe pain, (see below). If pain relief is adequate and there are no other acute complications, the patient can be discharged on oral analgesics. Other NSAIDs (ibuprofen, ketorolac {Toradol}, naproxen) are useful as adjunctive therapy to narcotics.
7. Give patients in moderate to severe pain an IV bolus of morphine 0.1–0.15mg/kg/dose (dose limit = 7.5mg). It can be repeated once, 60 minutes later, if pain relief is inadequate.
8. Start patients in severe pain on continuous morphine at 40µg/kg/h. Administer IV fluids to all patients in moderate to severe pain: a 10mL/kg bolus of saline, followed by 1.5 times the maintenance IV flow of 5% dextrose in normal saline.

Additional boluses of morphine, 0.05mg/kg, can be given q1–2h prn. If adequate pain relief is established for 2 hours with 1 or 2 doses of intermittent morphine, then consider administering acetaminophen with codeine (see above). These patients can then be discharged home, if they are able to take oral analgesics. Any patient requiring more than 2 doses of morphine should be hospitalized

9. Page and inform the Haematology consult service (see Introduction, Terminology section). The fellow shall see all seriously ill patients (see Introduction, Terminology section) and ensure that all admitted and discharged patients are followed up by the SCT.

Out-patient Management

Children should be discharged from ED on oral analgesics— acetaminophen (15mg/kg/dose) with codeine (1mg/kg/dose) po q4h for a period of 48 hours (acetaminophen max. 75mg/kg/day, and codeine max. 60mg/dose and 6mg/kg/day). Ibuprofen may be helpful (6 mos-12 yrs. 5-10mg/kg/dose po q6-8h, max. 40mg/kg/day or 2400mg/d). If pain persists after 48 hours, patients should be re-evaluated. The Haematology consult fellow (or, after hours, the

Haematology/Oncology fellow on-call) is to be notified of all children with sickle cell disease who have been assessed in the Emergency room and who will be discharged home. The SCT will follow up with the families the next regular working day; families should be advised to call the sickle cell nurse the following routine workday (Monday to Friday) at 416-813-6443. An instruction sheet (see Appendix 2) is to be given to the family upon discharge. A copy of the ED record shall be faxed to the office of the Sickle Cell Program (fax number, 416-813-5574).

In-patient Management—General Paediatrics (7B/C) Ward or Intensive Care Unit

Hospitalization is mandatory if pain control with oral analgesics is not adequate, or if other problems (such as fever or dehydration) exist.

1. Patients to be admitted to 7B/C under the General Paediatrics service. Patients should not be admitted to another ward (off-serviced). In certain cases, patients may be appropriate for transfer from the ED for admission to one of the partner hospitals with a satellite Sickle Cell Clinic (eg: Rouge Valley or William Osler Health Centre).
2. Analgesia: Continue IV morphine at 40µg/kg/h; if pain relief is inadequate, titrate the dose q8h by increments of 20µg/kg/h to a maximum of 100µg/kg/h. Boluses of morphine (0.05mg/kg) can be administered q1–2h prn for breakthrough pain. When effective analgesia is maintained for 24 hours, the dose can be decreased stepwise in 20µg/kg/h decrements q8h. For a pain crisis lasting more than 24–48 hours in a child older than 6 y of age, consider a PCA pump for patient-controlled analgesia. As well, consider a PCA pump for patients previously treated with a PCA pump or for patients not achieving adequate analgesia. A PCA pump delivers a continuous infusion plus IV boluses of a narcotic (morphine) on patient demand at a pre-programmed dose and interval. They can be obtained by paging the Pain Management Team at 416-235-8912, who will set the PCA's basal rate, bolus rate, and lockout time. While on morphine, patients should be observed carefully for signs of opioid toxicity: hypotension, bradycardia, drowsiness, coma, pinpoint pupils, cold clammy skin, and hypoventilation. The patient's heart and respiratory rate, and oxygen saturation should be continuously monitored and recorded. An equivalent dose of long-acting oral morphine may be used as an alternative to continuous IV morphine in stable in-patients. In a randomized study conducted at SickKids, po morphine was shown in sickle cell patients to be a reliable alternative to continuous IV morphine in the management of painful episodes. (Jacobson et al, 1997)
3. Administer a stool softener (eg: docusate sodium 5mg/kg/day, divided into three doses or as a single daily dose; usual adult dose, 100–200mg/day) unless the child has diarrhea. Antihistamines for pruritus may be given prn.
4. Hydration: Continue IV/po fluids at 1–1½ times the maintenance rate.
5. Studies do not support systematic use of oxygen for VOC. However, hypoxia may occur in children with VOC, resulting in increased sickling. Therefore, monitor O₂ saturation regularly and provide oxygen to patients exhibiting hypoxemia.
6. The usefulness of corticosteroids as an adjunct to reduce the duration of pain is unclear. Until the results of a satisfactory clinical trial are available, we suggest that corticosteroids not be used routinely.

7. Incentive spirometry is indicated for older children with chest or back pain: 10 breaths q1–2h while awake, or 5 breaths every 15 minutes (eg: with each TV commercial). The hospital's Child Life representative may also assist younger children with deep-breathing and blowing bubbles.
8. Observe patients closely for signs of deterioration: vital signs q4h, fluid input and output, and daily weight. Assess the child's comfort level q4h, and before and after each pain medication and non-pharmacologic intervention, with a consistent pain tool (that is, the Oucher or the 0–10 Verbal Report Scale; see Appendix 1). Encourage as much ambulation and activity as the child can tolerate.
9. Offer heating pads, massage, warm baths, and other comfort measures. The Child Life representative can recommend structured daily activity. Imagery and distraction are helpful. Request consultation with a physiotherapist as appropriate.
10. If pain is not managed despite appropriate analgesics or if complications result from pain, consult the Pain Management Team.
11. If the child is comfortable and has graduated to demand dosing only, switch to oral analgesics: acetaminophen (10-15mg/kg/dose) with codeine (1mg/kg/dose) tablet po q4h prn (acetaminophen max. 75mg/kg/day, and codeine max. 60mg/dose and 6mg/kg/day) given separately or together. Ibuprofen may be helpful (6mos-12yrs, 5-10mg/kg/dose po q6-8h, max 40mg/kg/day or 2400mg/d).
12. The SCT shall see the patient daily, Monday to Friday. In addition, the Haematology consult service must be formally consulted by General Paediatrics for any seriously ill or deteriorating patient.
13. When the patient is ready for discharge, inform the SCT, who will organize follow-up.

Discharge Criteria

- 1) The patient is tolerating fluids and medications by mouth.
- 2) Pain control is adequate with po medications.
- 3) Concurrent problems are resolved.

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Fever (Rule Out Infection) **Guidelines for Management in Children with Sickle Cell Disease**

Background

By 3–4 months of age (when fetal haemoglobin declines to <50% of total), many children with sickle cell anemia (HbSS) and sickle β -thalassemia develop clinically significant hemolytic anemia and impairment of splenic function. In others, although the HbF may remain above 50% these children are still at risk of splenic hypofunction. Even though the spleen may be enlarged during the first years of life, its phagocytic function is markedly reduced. Therefore, children with sickle cell anemia are at risk of overwhelming septicemia, often without a primary focus, due to encapsulated organisms, including *Streptococcus pneumoniae* and *Haemophilus influenzae* type B. If special measures are not taken, 15–20% of infants and young children with sickle cell anemia die before the age of 5, usually of septicemia or meningitis.

In children under 6 y of age with sickle cell disease, the predominant pathogen is *Streptococcus pneumoniae* (in 66%). In children over 6, gram-negative organisms account for over 50% of bacteremias. The incidence of pneumococcal bacteremia in children under 3 with sickle cell disease is 6 events per 100 patient-years. Furthermore, pneumococcal bacteremia carries a case fatality rate of about 20–25%. To reduce this high mortality, we strongly recommend:

- early diagnosis of sickle cell anemia and referral to a comprehensive care program for sickle cell disease.
- prophylactic penicillin, to be prescribed as soon as sickle cell disease is suspected, and continued until at least 5 years of age (to be continued past the age of 5 years in certain circumstances). In patients with significant beta-lactam allergy trimethoprim-sulfamethoxazole may be used, however, in view of multidrug resistant pneumococci an infectious disease specialist should be consulted.
- vaccination with Prevnar (7-valent) pneumococcal vaccine and the polyvalent (23-valent) pneumococcal vaccine (0.5mL subcutaneously or intramuscularly) and quadrivalent meningococcal vaccine (0.5mL subcutaneously) at 24 months of age (eg: ensure that the new conjugate pneumococcal and meningococcal vaccines as well as the HiB are started at 2 months or as soon thereafter as possible, especially if the family is immigrant or refugee).

Despite these measures, septicemia may still occur. Whenever a child with sickle cell disease has an oral temperature $>38.5^{\circ}\text{C}$, he or she should be seen urgently.

Emergency Department Treatment

Patients with sickle cell disease who present with fever of $\geq 38.5^{\circ}\text{C}$ (oral) or $\geq 37.5^{\circ}\text{C}$ (axilla) should be treated urgently.

1. Place the child immediately into an examining room, take a history, and do a physical exam, concurrently with other measures (see below). Note vital signs with O_2 saturation temperature, degree of pallor, spleen size, and any neurological deficits, jaundice, or respiratory distress.

2. Take blood for CBC, reticulocyte count, and blood culture. Ensure that sickle cell disease is written on laboratory requisitions and other tests as clinically indicated.
3. Intravenously inject ceftriaxone (Rocephin) 100mg/kg/dose (max. 2g/dose) through the same venipuncture as blood was taken. Ceftriaxone should be given within 30 minutes of presentation and before test results are available; intramuscular injection may be used if IV injection is not possible. Parenteral antibiotics should be given even if there is an obvious focus of infection (eg: otitis media, URTI, etc). If the patient is significantly allergic to beta-lactam antibiotics, (eg: anaphylaxis or other immediate hypersensitivity reactions or serum sickness) IV clindamycin (40mg/kg/day, divided q6-8h, max. 3.6g/day) can be used. Clindamycin is not to be used alone in the treatment of suspected meningitis, as it does not cross the blood–brain barrier. If the child is seriously ill (see Introduction, Terminology), add Vancomycin (60mg/kg/day, divided q6h, max. 4g/day).
4. Administer acetaminophen (15mg/kg/dose, q4h prn, max. 75mg/kg/day) or Ibuprofen (6 mos-12yrs, 5-10mg/kg.dose po q6-8h, max 40mg/kg/day or 2400mg/d).
5. Follow other critical-care pathways (protocols) for pain, acute chest, etc.
6. Other investigations may be indicated:
 - a) Chest x-ray, if the child has cough, hypoxemia, chest pain, or fever >40°C
 - b) Oxygen saturation
 - c) Monitoring arterial blood gases
 - d) Urine culture
 - e) Lumbar puncture
 - f) Blood typing and cross-matching (cross & type) if the child has pallor, respiratory or neurological symptoms, or splenic enlargement
 - g) Throat culture
 - h) Stool culture
 - i) Mycoplasma PCR from throat swab and Mycoplasma serology
 - j) Evaluation for osteomyelitis

Note: Prompt and careful physical examination and administration of IV antibiotics have high priority. **Do not wait** for chest x-ray or blood count results to administer antibiotics.
7. At this point, after a dose of antibiotic has been administered, page and inform the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call). He or she shall see all seriously ill patients and shall ensure that the SCT is informed of all patients seen in ED.

In-patient Management—General Paediatrics (7B/C Ward) or Critical Care Unit

Hospitalization is strongly recommended when the patient appears unwell, particularly in the presence of systemic toxicity, cardiovascular instability, and/or the following:

- The child's temperature is $>40^{\circ}\text{C}$.
- Recent doses of prophylactic penicillin have been missed.
- The child is under 1 year of age.
- There is respiratory distress.
- There is segmental/lobar infiltrate on chest x-ray.
- The child's WBC is >30 or $<5 \times 10^9/\text{L}$, Hb $<60\text{g/L}$, or platelets $<150 \times 10^9/\text{L}$.
- Family unable to purchase antibiotics.
- Follow-up is uncertain (distance, inconvenience, poor compliance) or the family's ability to cope is uncertain.
- The child has had previous episodes of severe sepsis or meningitis.

Empiric Therapy when meningitis is not suspected

Following initial emergency management, admit the patient to 7B/C under General Paediatrics. If the patient is stable and at low risk for sepsis, then consider transfer to one of the partner hospitals with a satellite Sickle Cell Clinic (eg: Rouge Valley, William Osler Health Centre.) If admitted to SickKids, these patients are **not** to be off-serviced (admitted) away from 7B/C.

1. Give IV cefotaxime (200mg/kg/day, divided q6–8h; max. 10g/day) until cultures are sterile and clinical status improves (minimum of 48 h). Patients with significant allergy to beta-lactam antibiotics, are to be treated with IV Clindamycin (40mg/kg/day, divided q6-8h; max. 3.6g/day). Clindamycin is **not** to be used in the treatment of meningitis, as it does not cross the blood–brain barrier.
2. In children 5 years of age or older with respiratory symptoms, administer Clarithromycin (15mg/kg/day po divided q12h, max. 1g/day). Erythromycin (40mg/kg/day IV divided q6h, max. 4g/day, or, po divided q6-12h as erythromycin estolate, max. 2g/day) may also be used. In children younger than 5 y of age, IV Clarithromycin/erythromycin may be given if suspicion of Mycoplasma.
3. Empiric treatment of presumed pneumococcal meningitis in sickle cell disease:

- Ceftriaxone (100mg/kg/dose, q12h x 3 doses than q24h, max. 2g/dose; 4g/day) plus Vancomycin (60mg/kg/day divided q6h, max. 4g/day)
- For significant allergy to beta lactam antibiotics use Vancomycin (60mg/kg/day IV, divided q6h, max. 4g/day) plus Rifampin (20mg/kg/day po, divided q12h, max. 1.2g/day).

Note: Antibiotics may be changed, once culture sensitivity results are available.

4. Give Vancomycin (60mg/kg/day, divided q6h; max. 4g/day) to patients who are severely ill (septic), in whom meningitis is suspected, or who deteriorate on cefotaxime/ceftriaxone. Decisions to stop Vancomycin must be made in consultation with Infectious Diseases.
5. Observe patients closely for any deterioration in clinical status, which may indicate septicemia or development of chest crisis.
 - a) Measure vital signs q4h.
 - b) Measure O₂ saturation continuously if the patient's O₂ sat <94%, or intermittently (q4-6h is suggested).
 - c) Administer O₂ to keep pulse O₂ ≥ 96%.
 - d) Administer IV fluids at 1.5 times maintenance for the first day (and while patients are febrile); then reduce to maintenance levels (po + IV).
 - e) Request blood cultures and CBC daily, if fever persists.
 - f) Request reticulocyte counts if haemoglobin is falling steadily.
 - g) If the patient has penicillin/cephalosporin-resistant pneumococcal meningitis, or is not improving after 36–48h of therapy, do a repeat lumbar puncture as an *in vivo* measure of treatment effectiveness.
 - h) If the patient is started on vancomycin, a trough level should be drawn prior to the 4th dose.
6. A representative (RN or MD) of the SCT shall see the patient daily, to maintain liaison with the clinic. The SCT representative shall discuss suggestions with the patient's attending physician, or a delegate, who will be responsible for writing specific orders. In addition, the Haematology consult service must be formally consulted by General Paediatrics for any seriously ill or deteriorating patient. Once the consult service is involved, all questions about hematological advice should go through the consult service fellow.
7. If the microbiology laboratory reports the 48h cultures as negative, stop antibiotics unless there is a focal infection or persistent fever. If the culture is positive and the organism is penicillin-susceptible, change to penicillin (250,000units/kg/day for non-meningitic infections or 400,000units/kg/day for meningitis, IV divided q4-6h, max. 24 million units/day). If the culture is positive for penicillin-non-susceptible pneumococcus, ensure that the patient is on Vancomycin, in addition to ceftriaxone/cefotaxime and consult Infectious Diseases.
8. When the patient is ready for discharge (see Discharge Criteria, below), inform the SCT, who will organize follow-up of the patient.
9. All in-patients seen during the week shall be signed out by the SCT or by the Haematology consult fellow at Friday afternoon Haematology/Oncology sign-out rounds.
10. The weekend on-call Haematology/Oncology team (staff physician and fellow) will consult on all ill children with sickle cell disease when requested.

Discharge Criteria

- 1) The patient is taking fluids and medications by mouth.
- 2) The patient is afebrile and well with negative cultures at 48h.
- 3) Pulmonary symptoms, if any, have resolved.

Out-patient Management

Out-patient management of sickle cell patients with fever is an area that is still being evaluated. A number of studies (Rogers et al. 1989; Wilimas et al. 1993; Williams et al. 1996) have reported the successful use of an out-patient approach in managing a selected group of well-appearing children with fever.

Two general approaches have been utilized in out-patient management: Following the initial dose of ceftriaxone, out-patients either (1) use oral antibiotics, or (2) return within 24 hours for a second dose of ceftriaxone. Each of these approaches has its advantages and disadvantages; both are clearly dependent on patient compliance.

Out-patient management of fever in sickle cell disease is an option *only when a number of safety checks are in place*. It is essential that all of four factors be in place prior to considering this approach:

1. Patients should be assessed and shown to be free of signs/symptoms of systemic toxicity other than fever.
 2. Patients should receive a broad spectrum, long-acting parenteral antibiotic (ceftriaxone).
 3. There is excellent patient understanding and compliance.
 4. Follow-up can be ensured.
- If **any** of these criteria are **not met**, then patient should be admitted for management.

1. Following the initial dose of ceftriaxone (in ED), if evaluation suggests that out-patient management is possible, a short period of observation (2–4h) is advised, followed by re-evaluation (assessment of vital signs, level of consciousness, and ability to take oral fluids/meds) prior to discharge.

Out-patient management should be considered on a case by case option only if the following criteria are met:

- The child's temperature is $<40^{\circ}\text{C}$.
- Recent doses of prophylactic penicillin have not been missed.
- The child is over the age of 1 year.
- WBCs are between 5 and $20 \times 10^9/\text{L}$; platelets $>100 \times 10^9/\text{L}$.
- There is no systemic toxicity and no other sickle cell complications.
- The patient has no respiratory distress.
- The child has received a dose of ceftriaxone.
- The family has a prescription for an oral antibiotic (see #2, see below) and there is no physician concern about the family's ability to obtain the prescribed medication.

- Follow-up can be ensured. Make note of patient and family compliance with therapy. Are there any psychosocial issues that may affect compliance with medication?
 - Verify that the telephone number available for the family is correct.
 - Make sure the family receives an Instruction Sheet (Appendix 2).
 - Ensure that the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call) has been informed of the case.
 - Verify that a copy of the ED record has been faxed to the office of the Sickle Cell Program (fax number, 416-813-5574), to ensure follow-up.
2. The patient should be given a prescription for a 3-day supply of oral antibiotic. We suggest either of the following:
- cefixime (Suprax: 8mg/kg/day, once daily, max. 400mg/day)
 - cefaclor (Ceclor: 40mg/kg/day, divided tid; max. 1.5g/day)

Acceptable alternatives include:

- a) cefprozil (Cefzil)
 - patients 6 mos to 12 years of age: 30mg/kg/day, divided bid, max. 1g/day
 - patients >12 years of age: 250–500mg bid
- b) Cefuroxime axetil (Ceftin) 30mg/kg/day divided bid (max. 1g/day) as suspension or 250mg bid in tablet form (tablets and suspension are not bioequivalent and suspension is very bitter)
- c) Clarithromycin (Biaxin: 15 mg/kg/day, divided bid; max. 1 g/day)
- d) Clindamycin 30mg/kg/day, divided q6-8h (max 1.8g/day)

Patients with significant allergy to beta-lactam antibiotics may be treated with clarithromycin or clindamycin. Duration of treatment depends on the findings at reassessment, including the focus of infection.

Other antibiotics used in other centres include amoxicillin and erythromycin-sulfamethoxazole. In making the recommendations above, we have weighed the risk of antibiotic resistance due to prior penicillin prophylaxis, the possibility of *Haemophilus influenzae* type B infection, and the incremental benefits of these agents in our setting in patients who have broken through on their penicillin prophylaxis.

Prior to discharge, verify:

3. That the Haematology consult service (or, after hours, the Haematology/Oncology fellow on-call) is informed and knows that the patient is being discharged. Have the emergency ward clerk fax the ED record to the office of the Sickle Cell Program (fax number, 416-813-5574).

That the parents have been advised to call the Sickle Cell Clinic the next workday (Monday to Friday) at 416-813-6443. Parents are to be given an instruction sheet (Appendix 2) and advised to resume penicillin prophylaxis when the antibiotic is completed.

Follow-up

The Haematology fellow shall inform the SCT (416-813-6443) that the patient was seen in ED, and of the patient's status. The next morning an update on the patient's status is to be done by telephone. This call shall be made by the SCT, Monday–Friday, or (for any patient discharged on Friday, Saturday, or holidays) by the Haematology/Oncology fellow on-call on weekends. In addition, the Sickle Cell Clinic should follow-up on day 3 following discharge, to ensure that there is compliance with medications and that the patient is well. They shall also check blood culture results.

Again, use caution in managing sickle cell patients with fever as out-patients. We suggest that only a small fraction of these patients are potentially suitable for this form of management. The strategy suggested above does not represent an exclusive course of action; it will be subjected to re-evaluation and prospective evaluation.

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Acute Chest Syndrome or Pneumonia Guidelines for Management in Children with Sickle Cell Disease

Background

Acute chest syndrome (ACS) is responsible for up to 25% of all deaths in children with sickle cell disease, and is the second most common cause for hospitalization in these children. The etiology of ACS is variable and may include both infectious and non-infectious causes; infections are more common in younger children. (Organisms include but are not limited to those listed below.)

Infectious Causes	Non-infectious Causes of ACS
<p>Bacteria</p> <p>Pneumococcus</p> <p>Gram-negative bacteria</p> <p>Chlamydia pneumoniae</p> <p>Mycoplasma pneumoniae</p> <p>Viruses</p> <p>Respiratory syncytial virus</p> <p>Para-influenza</p> <p>Influenza</p>	<p>Pulmonary infarction (<i>in situ</i> sickling)</p> <p>Hypoventilation secondary to rib/sternal infarction or narcotic administration</p> <p>Fat embolism</p> <p>Pulmonary edema secondary to fluid overload</p>

In patients with sickle cell disease, ACS occurs most frequently in patients with haemoglobin genotype SS (12.8 events/100 patient-years); less so in those with HbS β^0 thalassemia (9.4 events/100 patient-years) or HbSC (5.2 events/100 patient-years); and least often in those with HbS β^+ thalassemia (3.9 events/100 patient-years) (Castro et al. 1994). Within each Hb type, the incidence is strongly but inversely related to age, being highest in children 2–4 years old (25.3 events/100 patient-years) and decreasing to its lowest value in adults.

Clinical/Laboratory Features

Frequency of presenting symptoms in ACS appears to be age-specific. In young children (2-4 years old), fever and cough are typical; pain is rare; and upper lobe disease is more common. Adults tend to present with shortness of breath, chills, severe pain, and no fever; multi-lobe and lower lobe disease are more frequent.

Seasonal variation is seen, with more cases reported in the winter.

Tenderness may be present over the ribs or sternum. Chest x-rays of patients with ACS may show infiltrates in one or more lobes (66% of all presenting cases have single lobe involvement), but may also look normal or non-diagnostic in the first 2–3 days; pleural effusion may be visible in up to 30% of cases. Haemoglobin is often slightly lower than baseline (by a mean drop of 7g/L); leukocytes are often increased.

Emergency Department Treatment

Patients present to ED in various degrees of distress.

1. Place patients identified with a fever of $\geq 38.5^{\circ}\text{C}$ oral (37.5°C axilla) or who are in respiratory distress immediately into a room (see Fever/Rule Out Infection protocols).
2. Children without fever and breathing difficulties should be seen as soon as possible.
History: ascertain breathing difficulties; fever; nature, duration, and severity of pain; medications already used; associated symptoms; previous successful experience with analgesics; and previous episodes of ACS or pneumonia.
Physical: vital signs with O_2 saturation, cardiopulmonary and hydration status, spleen size, neurologic exam, presence of jaundice, and signs of infection.
3. Tests: Request CBC, diff, and reticulocyte count; blood culture, if the child is febrile; and continuous oxygen saturation monitoring if he or she is in moderate to severe respiratory distress. Request blood type and cross-matching (for possible exchange transfusion), if in respiratory distress.
4. Commence IV fluids at maintenance flow rate.
5. Take a nasopharyngeal swab in ED (before 11h00) or the next day on the ward.
6. Request chest x-ray and O_2 saturation if the child has fever, chest pain, tachypnea, or respiratory symptoms.
7. Administer oxygen to maintain O_2 saturation at $> 96\%$. Continuous monitoring of O_2 saturation is recommended.
8. See other protocols for fever, vaso-occlusive crisis, acute aplastic or splenic sequestration crisis, stroke, priapism, etc.
9. Place all patients admitted with ACS on IV cefotaxime (200mg/kg/day, divided q6–8h; max. 10g/day). May follow 24h after an initial dose of ceftriaxone in ED.

Treat all patients with appropriate hydration, analgesics, and antipyretics, in addition to other necessary investigations and treatment as per other protocols.

Page and inform the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call). The fellow shall see all seriously ill patients and ensure that all patients are followed up by the SCT.

In-patient Management-General Paediatrics (7B/C Ward) or Critical Care Unit

All patients with ACS should be hospitalized.

1. Admit to General Paediatrics (7B/C) or CCU, depending on severity of the case.
2. Administer hydration, analgesics, and antipyretics as necessary. Continue IV and po fluids at maintenance flow rates. Increase fluids as needed, if the child is dehydrated or insensible losses are increased (eg: persistent fever); excessive fluids, however, may precipitate or exacerbate ACS.
3. If signs (clinical or x-ray) of fluid overload are present, administer IV furosemide (Lasix 0.5–1mg/kg/dose, max. 60mg/dose).
4. If the child has a history of reactive airway disease or wheezing, consider bronchodilators (eg: Salbutamol {Ventolin}).
5. For the first 72 hours of admission, the patient should receive a third-generation cephalosporin (IV cefotaxime, 200mg/kg/day, divided q6–8h, max. 10g/day starting 24hr after the initial admission dose of ceftriaxone). Beyond 72h, some may be switched to cefuroxime (75 -150mg/kg/day IV, divided q8h, max. 6g/day), as follows:

Mild pneumonia & stable	Cefotaxime for 72h, then cefuroxime
Moderately severe pneumonia	Continue cefotaxime
Severe pneumonia or unstable	Cefotaxime + vancomycin 60mg/kg/day, divided q6h; max. 4g/day
6. Children ≥ 5 years of age should be suspected of having mycoplasma pneumonia; add Clarithromycin 15mg/kg/day po divided q12h (max. 1g/day) or Erythromycin (40mg/kg/day, IV, divided q6h; max. 4g/day or po as estolate, divided q6-12h, max. 2g/day). Use IV Clarithromycin in patients younger than 5 only if there is suspicion of mycoplasma. Patients with a significant beta-lactam antibiotic allergy can be treated with clindamycin (40mg/kg/day, IV, divided q6-8h; max. 3.6g/day); or 30mg/kg/day po (q6-8h max. 1.8g/day).
7. For children older than 4 years, consult a respiratory therapist for incentive spirometry: 10 breaths q1–2h when awake, or 5 breaths every 15 minutes, (eg: during every set of television commercials).
8. Encourage ambulation and activity. The hospital's Child Life representative can recommend structured daily activity.
9. Request a CBC daily with reticulocyte counts on Mondays and Thursdays during the hospital stay; and arterial/venous blood gases (ABG/VBG) daily, if not improving.
10. If the patient is started on vancomycin, a trough level should be done prior to the 4th dose.

11. For deteriorating patients (or patients transferred to the CCU), consider chest consultation (discuss need for tapping pleural effusion if present, need for V/Q scan and bronchoscopy).
12. Transfusion guidelines (see also the Transfusion protocol): The Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call) shall be consulted about all patients being considered for transfusion.
 - Patients with mild to moderate disease and haemoglobin (Hb) at baseline do not generally need a transfusion.
 - Patients with moderately severe disease and Hb 15g/L less than baseline should be transfused with packed RBCs, 10mL/kg (simple transfusion). Patients should not be transfused to a Hb of greater than 100g/L (Hct >30%).
 - Patients with severe disease—extensive infiltrates; worsening ABGs; increasing need for oxygen (>40% O₂) and decreasing O₂ saturation; need for CCU; etc.—should have an exchange transfusion (RBC cytapheresis).
13. A SCT representative and the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call) shall see the patient daily. Any child admitted with ACS is ill by definition and hence requires a formal Haematology consult. These patients are to be signed off to the Haematology/ Oncology fellow on-call every evening and on weekends or holidays.
14. When ready for discharge, the SCT shall be informed; they will organize patient follow-up.

Discharge Criteria Guidelines

- 1) The child does not require supplemental oxygen.
- 2) The patient has been afebrile for at least 24 hours.
- 3) The child is taking fluids and medications by mouth.
- 4) Pain control is adequate with po medications.
- 5) Concurrent problems are resolved.

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Aplastic Crisis

Guidelines for Management in Children with Sickle Cell Disease

Background

Aplastic crisis, an acute complication in sickle cell disease and other hemolytic anaemias, occurs when red cell production is temporarily reduced while the ongoing hemolytic process continues, resulting in severe anaemia. The condition is characterized by a rapid fall in haemoglobin (the reticulocyte count falls to <0.1%; Hb falls often to 30–50g/L) from a direct effect of parvovirus B19 or (rarely) other infectious agents on erythroid progenitors in the marrow. Aplasia is usually limited to 7–10 days; but because this may exceed the patient's mean erythrocyte survival time, profound anaemia may ensue, leading to death unless the patient is transfused. After 7–10 days, patients develop an antibody response resulting in viral neutralization and resumption of "normal" marrow erythroid activity. This is heralded by the appearance of large numbers of nucleated RBCs on the blood smear. Patients with HbSC and sickle β^+ thalassemia are less severely affected.

The transfusion of a patient in aplastic crisis, although potentially life-saving, may result in cardiac failure in patients with very low haemoglobin. For patients showing evidence of cardiac failure, transfusions are best undertaken as partial isovolumic red-blood-cell exchange.

Parvovirus is very contagious and poses a risk to siblings with sickle cell anaemia and to pregnant health-care providers who are not immune. A sibling with sickle cell disease who has not had a documented aplastic crisis should have a haemoglobin and reticulocyte count checked, initially and repeated in 10–14 days. In the hospital or clinic, a child with aplastic crisis should be placed in contact isolation. As soon as there is evidence of the disease resolving (eg: a rise in reticulocyte count), the child is no longer infectious.

Clinical Features

Patients usually present with fever, malaise, lethargy, and possible syncope due to anaemia. Physical examination shows pallor, tachycardia, and symptoms of congestive heart failure. The spleen is not generally larger than usual.

Management

1. In ED, conduct a history and physical exam. Note vital signs and any presence of postural BP instability, a cardiac gallop, enlarged liver, or other signs of congestive heart failure. Where possible, determine the patient's baseline Hb concentration (for many patients, it will be available through the "EPC" and "KidCare").
2. Tests: CBC, diff, reticulocyte count, blood type and cross-match, and parvovirus and Epstein-Barr virus serology (acute and convalescent).

3. Transfusion is required if the patient is symptomatic and has no signs of bone marrow recovery (no nucleated RBCs in a peripheral blood smear, and/or reticulocyte count <1%). Transfuse (see Transfusion protocol) 10 to 15mL of packed RBCs per kilogram of body weight; transfuse slowly, by dividing packed RBCs into aliquots of 5–7mL/kg and serially transfusing each over 4 hours. Furosemide (0.5mg/kg, midway through the transfusion) may be required. Watch for fluid overload. Transfuse slowly, with a diuretic.
4. Inform the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call) of any patient with sickle cell disease presenting to ED who is unstable or who requires transfusion based on a low haemoglobin measurement.
5. Start transfusing in ED if the patient is unstable (eg: has postural BP instability, enlarged liver, cardiac gallop). If the patient is stable, transfusion can be delayed a few hours and commenced on the ward.
6. On General Paediatrics (7B/C Ward) or in the CCU, commence (or continue) blood transfusion. The child should be hospitalized for 24h unless other reasons justify longer hospitalization. Following transfusion and observation for 24h, patients can be discharged with follow-up to be arranged by the Haematology consult fellow through the SCT.
7. Haemoglobin and reticulocyte count should be followed every 2–3 days as an out-patient until the reticulocyte count rises and Hb increases, whether a transfusion was given or not. This will be arranged by the SCT.
8. Place in-patients in contact isolation. As parvovirus can cause miscarriage (hydrops fetalis), patients should have no contact with pregnant hospital personnel.
9. Fever during an aplastic crisis is most likely due to parvovirus infection, but patients should still have a blood culture and receive parenteral antibiotics according to the Fever protocol.

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Acute Splenic Sequestration Crisis Guidelines for Management in Children with Sickle Cell Disease

Background

By 4–5 months of age, splenomegaly develops in some infants with sickle cell disease, and by 12 months of age a palpable spleen is noted in nearly half. Although enlarged, the spleen does not properly perform its filtration function. However, its reservoir function is overactive: sequestration of large quantities of blood (often half or more of a child's blood volume) can occur rapidly. This complication, termed acute splenic sequestration crisis (ASSC), is characterized by pooling of large quantities of sickled RBCs in the splenic red pulp, sudden enlargement of the spleen (within hours), and a precipitous decline in haemoglobin (Hb) and possibly platelets.

Attacks of ASSC are often (60%) associated with episodes of fever, suggesting an underlying viral etiology. ASSC occurs most commonly in infants and young children between 6 months and 5 years of age with sickle cell anaemia. It may also occur in older patients with HbSC disease, sickle β thalassemia, sickle β^+ thalassemia, or SS genotype patients with chronic splenomegaly (often patients with concomitant β -thalassemia). There is usually no obvious triggering event.

Clinical/Laboratory Features

A child with an acute splenic sequestration crisis presents with symptoms of

- acute anaemia (pallor, tachycardia, frank cardiovascular collapse);
- splenomegaly (pain in the left upper quadrant, thrombocytopenia); and
- evidence of an active bone marrow response (increased reticulocytes).

Retrospective reviews have shown a first-episode mortality of as much as 14%. On physical examination, patients show signs of anaemia, hypovolemia, and an enlarged spleen (larger than baseline), sometimes massively so. Mild cases may be asymptomatic.

Haemoglobin concentration is at least 20g/L below the baseline steady state. In severe cases, haemoglobin may decline to life-threatening levels. Reticulocyte counts are usually elevated, which distinguishes this condition from aplastic crisis. The platelet count often declines to $<50 \times 10^9/L$.

The mainstay of ASSC management is transfusion, to provide circulating erythrocytes and volume. Risk of recurrence is approximately 40–50%, usually within 3 years. Because it is not possible to predict which children will have recurrent attacks, most experts recommend splenectomy after the first major attack (for patients >2 years old), or chronic transfusion to maintain a haemoglobin S level under 30% (for patients <2 years), which may allow postponement of splenectomy until the age of 2 years. Unfortunately, recurrent attacks have occurred in patients on chronic transfusions despite HbS levels $<30\%$, suggesting that this mode of therapy is of value only in young children, who because of age are at a substantial risk of infection if splenectomized.

Emergency Department Treatment

1. Conduct a history and physical exam with emphasis on signs and symptoms of cardiovascular collapse (shock), anemia, and hypovolemia. If the spleen is palpable, verify with the parent, and chart that it is larger than normal.
2. Tests: CBC, diff, reticulocyte count, blood type and cross-match, O₂ saturation and ABG. Establish IV access.
3. In mild cases (which are uncommon) of ASSC (eg: spleen only slightly larger than usual, Hb <15g/L below baseline, patient haemodynamically stable), the child may be closely followed as an out-patient. Prior to discharging, inform and discuss the case with the Haematology consult service (or, after hours, the Haematology/ Oncology fellow on-call). The fellow will leave a message with the SCT. Reinforce with parents how to palpate their child's spleen and indicate to them that if the spleen is enlarged or if the child's condition deteriorates in any way that they are to return immediately to the Emergency Department. The SCT will follow up the next day. It would be reasonable to admit all patients with ASSC if follow-up is in doubt (on or just before a weekend, where there are questions of patient/family compliance, etc.).
4. Patients with more severe ASSC (most patients) should be admitted to the General Paediatrics Ward (7B/C), or to the CCU if unstable, following a discussion with the Haematology consult fellow (or the Haematology/Oncology fellow on-call after hours), who should notify the SCT by telephone (416-813-6443).

In-patient Management

1. While the child is an in-patient, take vitals (q2–4h), careful repeated physical assessments (q4–6h) for spleen size (measure with tape and record), and Hb measurements (q8–12h). The patient's heart and respiratory rates and O₂ saturation should be recorded on a monitor. Patients should be on a cardiac or O₂ monitor.
2. To raise the haemoglobin and maintain cardiovascular stability, transfuse the patient with 10–15mL/kg of packed RBCs if there are any signs of cardiovascular collapse or if Hb levels are less than 40–50g/L (repeat if necessary). Time permitting, use available phenotypically matched (sickle-negative) blood. Aim for a Hb of 80–90g/L.
3. In hospital, continue regularly scheduled medications.
4. Administer oxygen to keep O₂ saturation >96%.
5. An acute sequestration episode usually resolves within 2–5 days. When there is evidence of rising haemoglobin and diminishing spleen size, the patient can be discharged, with close out-patient follow-up by the SCT.
6. For weeks-months following an episode of ASSC, some patients have persistent splenomegaly and hypersplenism, with lower-than-usual Hb and platelet values.

7. Recurrent episodes requiring transfusion should be treated with splenectomy if the child is over 2 years of age, or with chronic transfusions if 2 years old or less. Any patient who presents to the hospital with a recurrent episode of ASSC should be seen by the General Surgery consult service. The request for a General Surgery consultation is to be made by the General Paediatrics service in consultation with the SCT or the Haematology consult fellow. The patient should receive vaccinations for encapsulated organisms (pneumococcus, meningococcus, and Haemophilus type B); these will be done in clinic.

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Stroke

Guidelines for In-patient Management in Children with Sickle Cell Disease

Background

Stroke (CVA) occurs in 5–10% of people with sickle cell anaemia (HbSS disease), but can also occur in those with $S\beta^0$ and $S\beta^+$ thalassemia and HbSC disease. The risk of CVA is highest in such children between 1 and 9 years of age. Infarctive strokes are more common in children, whereas hemorrhagic strokes occur more frequently in adults (ages 20–29). Marked narrowing (to complete occlusion) of the anterior or middle cerebral arteries are the most common abnormalities found in children.

Thrombosis and intimal hyperplasia, the precursors of infarctive stroke, are thought to result from a combination of factors seen in sickle cell disease. These include high blood-flow velocity in cerebral vessels, rigidity of circulating RBCs, adherence of RBCs to vessel walls, and intravascular sludging. Stroke occurs when the narrowing is severe enough to compromise distal flow, or a thrombus dislodges and causes distal embolization. Hemorrhagic strokes are thought to result from tears in over-dilated vessels. The risk of infarctive strokes correlates with severity of disease, previous stroke, silent infarction on MRI, sickling with h/o stroke, HbS concentration, severity of anaemia, and elevated transcranial doppler velocity. Without treatment, $\frac{2}{3}$ of patients with CVA will have recurrent strokes, usually within 3 years. The recurrence rate is reduced significantly by a chronic transfusion program (maintaining a level of haemoglobin <30%).

Clinical Features

Ischemic stroke typically presents with signs and symptoms of hemiparesis or hemianaesthesia, visual field deficits, aphasia, cranial nerve palsies, or acute change in behaviour. Hemorrhagic strokes present with more generalized phenomena such as coma, headaches, and seizures. Transient ischemic attacks (TIA) are defined by neurological signs that resolve within 24–48 hours; they often occur before an infarctive stroke, but may go unnoticed in young children.

Laboratory Features

A computed tomographic scan (without contrast) requested in the emergency room may appear normal, whereas a CT done 2–7 days post-CVA usually shows areas of infarction. MRI/MRA is very sensitive in detecting intracranial hemorrhage or infarction.

Emergency Department Treatment

1. If CVA or meningitis is suspected, place patient immediately into a room, and assess as soon as possible.
2. Stabilize vital signs and life support as necessary.
3. Treat seizures and increased intracranial pressure, if present.

4. Conduct a history and physical exam concurrently with other measures.
History: quality, timing, severity, and duration of headaches; previous headaches; nausea or vomiting; drooling; visual changes; paresis; loss of coordination; parasthesias; fever; syncope; seizures; recreational or prescribed drug use.
Physical: vital signs, detailed neurologic exam, hydration status, spleen size, presence of jaundice, signs of infection, etc.
5. Tests: CBC, diff, reticulocyte count, electrolytes, magnesium, calcium, phosphate, blood typing and cross-matching, blood and urine cultures if patient is febrile, lumbar puncture if meningitis is suspected. Blood for coagulation screen (INR, aPTT). Send extra “coag tube” for rest of coagulation work-up: antithrombin III, protein C, protein S, plasminogen, APC resistance, antiphospholipid antibody, anticardiolipin antibody. Establish an IV at maintenance flow rates.
6. If the child is febrile, immediately administer cefotaxime (200mg/kg/day; divided q6-8h, max. 10g/day) or (ceftriaxone 80mg/kg/dose; max. 2g/dose). Add IV vancomycin (60mg/kg/day; divided q6h, max. 4g/day), if the child is septic or meningitis is likely. Patients with significant allergy to beta-lactam antibiotics can be treated with IV clindamycin (40mg/kg/day, divided q6-8h, max. 2.7g/day) [For Fever only]. For Sepsis or meningitis in children with beta-lactam allergy refer to Fever Protocol.
7. Administer oxygen to maintain O₂ saturation >96%.
8. Keep NPO, head of bed flat.
9. Maintain normothermia ~ head temperature > 37°C.
10. Ensure normal blood pressure. Control blood pressure if necessary with medication or fluids.
11. See other critical pathways (protocols) for fever, VOC, etc.
12. Page and inform the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call). The fellow shall see all sickle cell patients with stroke and discuss with Haematology responsible staff.
13. The transfusion will take place in the CCU, but preparations will begin in ED.
14. The Haematology fellow informs the blood bank of required packed red cell volume and discusses with the dialysis nurse on-call.

In-patient Management—Critical Care Unit

1. Admit to CCU.
2. Request MRI and MRA. If these tests are not immediately available, arrange for a CT without contrast, to exclude intracranial hemorrhage.

3. If the patient is febrile, administer cefotaxime (200mg/kg/day IV, divided q6–8h; max. 10g/day). If the patient has a significant allergy to beta-lactam antibiotics, give IV clindamycin (40mg/kg/day, divided q6-8h; max. 2.7g/day). Clindamycin is not to be used alone in the treatment of suspected meningitis, as it does not cross the blood–brain barrier; if meningitis is suspected, add IV vancomycin (60mg/kg/day, divided q6h; max. 4g/d). In patients with significant allergy to beta-lactam antibiotics, treat meningitis with vancomycin and rifampin (see Fever protocol); consult with Infectious Diseases.
4. Continue IV fluids at maintenance flow rates.
5. For diagnosed CVA, and/or clear history/physical indicating CVA, perform double-volume RBC exchange transfusion to a haemoglobin of 100g/L if possible and HbS level of <30% of total Hb (see Transfusion protocol). Remove the central venous line as soon as possible after the blood exchange, to reduce the risk of thrombosis.
6. Consult with Neurology for baseline assessment and follow-up once CVA is suspected.
7. Consult with physical and occupational therapists after exchange when patient is stable.
8. Order a hypercoagulable work-up (protein C, antithrombin III, etc.).
9. Order ECG, ECHO.
10. Where possible encourage ambulation and activity. The hospital's Child Life representative can recommend structured daily activity.
11. A member of the SCT (RN or MD) shall see the patient daily.
12. When the patient is ready for discharge, inform the SCT; they will organize clinic follow-up and the next transfusion.

Discharge Criteria

- 1) The patient has been clinically and neurologically stable for at least 48 hours post transfusion(s).
- 2) The child has been afebrile for at least 24 hours.
- 3) The child is taking fluids and medications orally.
- 4) Haematology, stroke seizure and physical therapy follow-up has been organized.
- 5) A plan for chronic transfusion program has been initiated.

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Priapism

Guidelines for Management in Children with Sickle Cell Anemia

Background

Priapism, a painful, prolonged (>30 minutes) erection of the penis, has been found to occur at least once in 75% of males with sickle cell anaemia before the age of 21 years. There are two bimodal peaks (ages 5–13 and 21–29y). In a majority of cases, priapism occurs during early-morning sleep and awakens the patient. Sexual activity is a precipitating event in approximately 20% of cases; however, in 40% of cases no provoking event is identified. Priapism occurs in two forms: stuttering, which lasts 2h or less, and severe, which lasts more than 2h and may result in impotence.

The pathophysiology of priapism in sickle cell disease remains elusive. It is thought that the relative stasis of blood within the corpora during normal erection decreases the oxygen tension and pH, both circumstances conducive to sickling. Sickling of RBCs and sludging of blood within the corpora leads to further hypoxia and acidosis, which in turn promotes further sickling.

Eventually an inflammatory response is elicited, resulting in fibrosis; it is this that ultimately is responsible for impotence. Priapism is more common in patients with SS disease, but can also occur in those with SC disease or S β thalassemia.

The best treatment for priapism in patients with sickle cell disease is not known. Analgesia and hydration are of benefit, but the role of transfusion (if any) or surgery is not clear. Positive prognostic predictors in priapism include being prepubertal, early presentation, and early treatment. In managing priapism, one should distinguish stuttering priapism from the severe form. In stuttering priapism, no specific intervention is required for a single episode: Simple treatments such as hydration, warm baths, and analgesics are usually sufficient to end it. Severe or prolonged events (>2h) are to be considered emergencies requiring prompt medical intervention.

Management

1. Rapid triage - place immediately into exam room.
2. Tests: CBC, reticulocyte count, blood typing and extended cross-matching. Urine - routine analysis and culture. Blood cultures if febrile (see Fever protocol).
3. Administer IV fluids: a 10mL/kg bolus over 1h, followed by 1.5 times the maintenance flow rate.
4. Give patients in moderate to severe pain an IV bolus of morphine 0.1–0.15mg/kg/dose (dose limit = 7.5mg). It can be repeated once, 60 minutes later, if pain relief is inadequate.
5. Consult anaesthesia to request an epidural to improve pain control if inadequate pain control with IV morphine.
6. Administer 1 dose of po pseudoephedrine (30mg for children <12 years of age; 60mg for patients >12y of age).

7. Ice or cold packs should **NOT** to be used. Sitting in a warm bath can be helpful.
8. Oxygen by nasal cannula/face mask to monitor O₂ saturation >96%.
9. After 2h, if priapism continues despite analgesics, hydration, and pseudoephedrine, request urgent Urology and Haematology consultations.
10. The Urology fellow shall advise on whether to do penile aspiration–drainage and irrigation with epinephrine.
11. After 12h, if there is no evidence of detumescence, do an exchange transfusion to reduce HbS <30%.
12. For recurrent priapism, discuss the use of GnRH analogues (Lupron, injected intramuscularly every month) with a consultant from Urology.

Discharge Criteria

- 1) The priapism is resolving (complete detumescence may take 1–2 weeks).
- 2) The child is afebrile.
- 3) The child is taking fluids and medications orally.
- 4) Pain relief is adequate.
- 5) For recurrent priapism continue pseudoephedrine (30mg po qhs in children 12y of age; 60mg po qhs, if >12y old).

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Gallstones

Guidelines for Management in Children with Sickle Cell Disease

Background

In sickle cell disease, erythrocyte haemolysis is increased, resulting in increased serum bilirubin. This is most evident in children with sickle cell anaemia and $S\beta^0$ thalassemia, and to a lesser degree in SC disease. This often leads to cholelithiasis (gallstone formation) and cholestasis.

Clinical/Laboratory Features

In patients with SS and $S\beta^0$ thalassemia, gallstones are found in approximately 14% of children under 10 years of age, about 30% of adolescents, and 75% of adults over 30. The incidence is lower in patients with SC disease or $S\beta^+$ thalassemia. Gallstones may be asymptomatic or cause symptoms such as early satiety, nausea, vomiting, and pain in the right upper quadrant (RUQ). Patients may report changes in the colour of the sclera, skin, stool, and/or urine. Abdominal pain in children with sickle cell disease may have many causes:

- vaso-occlusive crisis
- acute hepatic crisis
- liver sequestration
- pancreatitis
- urinary tract infection
- cholecystitis
- splenic sequestration
- appendicitis
- acute chest syndrome
- pelvic inflammatory disease

Complications of cholelithiasis include:

- acute cholecystitis
- acute pancreatitis
- acute cholangitis
- common bile duct obstruction

Distinguishing acute cholecystitis and cholangitis from acute hepatic sequestration is difficult and may be possible only with ultrasound and other hepatic scans. Cholangitis is usually diagnosed by the combination of fever (septic appearance), jaundice, and RUQ pain, in combination with gallstones.

Gallstones may be visible on plain x-ray but are best seen with abdominal ultrasound. Most stones are radiopaque. Ultrasound can also detect biliary sludge, a deformed or thickened gallbladder wall, and changes in the calibre of the common bile duct.

The degree of cholestasis and obstructive jaundice is reflected in blood concentrations of direct bilirubin (conjugated), and the degree of elevation of alkaline phosphatase and γ -glutamyltransferase (GGT).

Asymptomatic gall stones are left alone.

Emergency Department Treatment

Patients present to ED in various degrees of distress.

1. Patients with fever of $\geq 38.5^{\circ}\text{C}$ or who are in respiratory distress should be assessed immediately. After antibiotics have been administered (as per Fever protocol), assess pain thoroughly. Follow protocols for VOC, ACS, etc., as needed.
2. Conduct a history and physical exam concurrently with other measures.
History: nature, duration, and severity of pain; medications already used, and previous use of analgesics; changes in the colour of the sclera, skin, stool, and/or urine; associated symptoms; breathing difficulties; fever.
Physical: vital signs, presence of jaundice, cardiopulmonary and hydration status, spleen size, neurologic exam, signs of infection, etc.
3. Tests: CBC, diff, reticulocyte, bilirubin (conjugated and unconjugated), alk phos, GGT, AST, ALT. If the child is dehydrated, start IV fluids at the maintenance flow rate. Patient should be made *npo*.
4. Request an abdominal ultrasound.
5. Page and inform the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call). The fellow shall see all seriously ill patients and ensure that all patients are followed up by the SCT.
6. Administer analgesics as needed (see management guidelines for acute painful episodes).
7. Administer ampicillin, gentamicin, and metronidazole for suspected cholangitis. If patient has a significant allergy to beta-lactam antibiotics administer vancomycin, gentamicin and metronidazole. Discuss all cases of suspected cholangitis with the General Surgery consult service.

In-patient Management—General Paediatrics (7B/C Ward) or Critical Care Unit

All patients with acute cholecystitis should be hospitalized for monitoring, IV fluids, antibiotics, and analgesics.
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If elective cholecystectomy is planned, it should be performed after the acute attack has subsided. Laparoscopic cholecystectomy has replaced the open procedure in most cases. Emergency surgery should be avoided, unless the patient shows evidence of obstruction of the common bile duct.

1. Admit patients to General Paediatrics (7B/C) or CCU, depending on severity. Patients should not be off-serviced (admitted to other wards).
2. Consult with the Gastroenterology service if an obstruction is suspected, or when LFT results are notably abnormal compared to baseline (see old chart for baseline). Arrange (through the GI/Nutrition service) for endoscopic retrograde cholangiography (ERCP), if ultrasound suggests that an obstruction is present.

3. Discuss open vs. laparoscopic cholecystectomy with the General Surgery consult service; it is best scheduled for when the child is not acutely ill. Do pre-operative planning for elective procedures in consultation with the SCT (see Peri-operative Management guidelines). Patients with suspected cholangitis must be seen urgently by General Surgery.
4. Continue analgesia (see pain management protocol about analgesia, stool softeners, antipruritics, etc.)
5. Observe patients closely for signs of deterioration of clinical status. Assess vital signs q4h, and weight and fluid daily. Assess comfort level with a consistent pain tool (eg: the Oucher or the 0–10 Verbal Report Scale) every shift, and before and after administering pain medications.
6. Administer IV and po fluids at the maintenance flow rate. Increased fluids may be needed if the child is dehydrated or insensible losses are increased (eg: fever).
7. In children >4 years of age, request a respiratory consult for incentive spirometry.
8. Encourage ambulation and activity. The hospital's Child Life representative can recommend structured daily activity.
9. A representative of the SCT shall see the patient daily (Monday-Friday). Consult the Haematology service (or, after hours, the Haematology/Oncology fellow on-call) about any seriously ill or deteriorating patient.
10. Inform SCT when the patient is ready for discharge; they will organize follow-up. Follow-up with general surgery, however, shall be arranged by the ward; inform SCT of this, as well.

Discharge Criteria

- 1) Bilirubin levels have returned to baseline.
- 2) The child has been afebrile for at least 24 hours.
- 3) The child is taking fluids and medications orally.
- 4) Pain relief is adequate with po medications.
- 5) Concurrent problems have resolved.

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Transfusions

Guidelines for Management in Children with Sickle Cell Disease

Background

RBC transfusions are an integral part of the management of sickle cell disease. Transfusion of normal (non-sickle) blood into patients with sickle cell disease increases hematocrit (Hct) and simultaneously (by dilution) lowers the fraction of cells that contain HbS. By increasing Hct, transfusion may also reduce the erythropoietic drive and decrease production of sickle haemoglobin. Finally, HbS can be “replaced” with HbA by exchange transfusion. Thus, the end result of transfusion by any method is some combination of an increased Hct and a decreased proportion of erythrocytes that contain HbS. The goal of such therapy is to improve O₂ carrying capacity and/or prevent sickle-related vascular events.

O₂ delivery is a function of the interaction of Hct, blood volume, viscosity, vascular perfusion, and other factors such as haemoglobin–oxygen affinity. The primary determinants of blood viscosity are Hct and RBC deformability. Increases in Hct, although beneficial in improving O₂ delivery, eventually are counterbalanced by an opposing detrimental increase in viscosity. The optimal transfusion is one that improves O₂ delivery with an isovolumic exchange transfusion (fixed Hct), eg: an exchange transfusion. Unfortunately this type of transfusion is more costly and labour-intensive, and exposes patients to a higher risk of transfusion complications (infections, alloimmunization, need for a central venous line, etc.).

In general, acute simple transfusions are indicated when increased O₂ carrying capacity is desired, but no great decrease in HbS is required. Such transfusions should be considered in patients with symptomatic anaemia—in acute splenic or aplastic crises, cases of blood loss, and possibly in pre-operative preparation. In these conditions, the rapidity of transfusion should be guided by the clinical state of the patient. A prudent course is to give small amounts of red blood cells slowly. To avoid unnecessary exposure, a unit of blood may be subdivided into smaller aliquots. A helpful rule in determining the volume of blood cells to be transfused is to begin with the same number of millilitres per kilogram of body weight as the haemoglobin level in g/dL; for example, a patient with a Hb of 5g/dL (50g/L) would initially receive 5mL/kg of erythrocytes.

Transfusion is generally not required in the management of routine, uncomplicated, painful crises.

There is good evidence that chronic simple transfusions to maintain HbS < 30% are valuable to prevent recurrent strokes or after an initial CVA or for primary prevention in patients shown to be at risk by having elevated transcranial doppler velocity. Other indications for chronic transfusion are selected patients with severe, recurrent, debilitating symptoms such as painful crises, leg ulcers, and priapism may benefit from short courses of transfusion. Chronic transfusion has been used in young children with sequestration crises in an attempt to delay or avoid splenectomy, as well as in patients with recurrent acute chest syndrome, chronic pulmonary disease, and symptomatic congestive heart failure.

RBC exchange transfusion offers potential advantages over simple transfusion for the management of certain complications of sickle cell disease. It allows the Hct and HbS to be adjusted rapidly and simultaneously, without incurring the risks of increasing blood viscosity and blood volume. The major role for exchange transfusion is in the management or prevention of life- or organ-threatening events. Unfortunately, randomized trials in such settings have rarely been possible; indications for exchange are therefore based largely on anecdotal reports.

Conditions for which relatively good evidence exists for the use of exchange transfusions include acute chest syndrome (ACS) and acute or impending CVA. Anecdotal success with exchange transfusion has been reported in the management of priapism failing to respond to 12–24 hours of conservative management with IV hydration, narcotics, and supplemental O₂.

There remains controversy about the optimal pre-operative management of sickle cell disease (see perioperative guidelines). For most minor elective surgical procedures, no transfusion is needed; whereas for major procedures (thoracotomy, laparotomy, tonsillectomy/adenoidectomy), or procedures in children suffering from intercurrent illnesses, pre-operative transfusion has a definite role. Because of the increased risk of transfusion complications associated with exchange transfusions, for most procedures pre-operative exchange transfusion holds little benefit over simple transfusion.

Complications of transfusion therapy, both acute and chronic, are numerous. Chronic complications such as alloimmunization, iron overload, viral infection, and hypersplenism are beyond the scope of this report. Acute complications that should be considered when transfusing these patients are hyperviscosity and transfusion reactions. When transfusing patients with sickle cell disease, Hct should not be allowed to increase above 35% (about 110-120g/L), to avoid the potentially detrimental effects of hyperviscosity.

Management: Practical Transfusion Issues

1. Prior to transfusion, ensure that the following tests have been performed: CBC, reticulocyte count, Hb electrophoresis (if not already done), red cell phenotype, screen for alloantibodies, blood grouping and cross-matching, and O₂ saturation or ABGs.
2. Discuss with the Haematology consult fellow (or, after hours, the Haematology/Oncology fellow on-call) the indications for transfusion and the type of transfusion (simple or exchange) to be done. A Haematology consult is mandatory for exchange transfusion.

For RBC apheresis, the Haematology consult fellow (or on-call fellow) shall:

1. Calculate the amount of blood to be given, according to the formula below.
2. Inform the blood bank and provide the following information: that you plan an RBC exchange in the next few hours; the patient's name, sex, height, weight, and Hct; and the desired amount of blood to be transfused.
3. Arrange for CCU admission (call 416-813-6486). Ask the CCU staff to place a double-lumen central line (usually a femoral Quinton). Interventional radiology staff may be requested to place the line during daytime hours if scheduling permits.
4. The first call should go directly to the apheresis/dialysis nurse on-call. She will call Dr. Geary or delegate if she has a scheduling conflict or staffing issue or other concerns.

Calculation of RBC volume required for transfusions

See the Glossary of Abbreviations for any terms not defined below.

Hctd	=	desired hematocrit
Hcti	=	initial (patient's) hematocrit
Hctrp	=	hematocrit of replacement fluid; Hctrp of packed RBCs = 70–80%
TBV	=	total blood volume (in millilitres), which can be calculated as: For neonates: patient's weight X 100mL/kg One month to 10 years of age: patient's weight X 80mL/kg Older than 10 years: patient's weight X 70mL/kg

Simple Transfusion (not exchange)

$$\text{Packed RBC volume (mL)} = \frac{(\text{Hctd} - \text{Hcti}) \times \text{TBV}}{\text{Hctrp}}$$

A transfusion of 10mL/kg is usually sufficient.

Chronic Simple Transfusion

A transfusion of 10–15mL/kg of packed RBCs every 3–5 weeks is usually sufficient to maintain HbS near 30% and the pre-transfusion Hct between 25% and 30%.

Exchange Transfusion

Double-volume RBC exchange = 2 X (Hcti X TBV)
(A double-volume exchange transfusion usually lowers HbS to approximately 10%.)

Selection and Preparation of Blood

Emergency simple transfusion (eg: for an aplastic or sequestration crisis): Use AS-3 RBCs (not necessarily sickle-negative blood) up to 35 days old, plasma-depleted (hematocrit 0.7 to 0.75); cross-match compatible for Rh and Kell antigens if possible.

Planned simple (long-term) transfusion: AS-3 red cells up to 35 days old, plasma depleted, matched for extended phenotype: minimum Rh and Kell, Kidd (Jka, Jkb), Duffy (Fya), and S (of the MNS system) if possible.

All transfusion reactions must be reported to the Blood Transfusion Laboratory. Transfusion Medicine will record the frequency and severity of reported transfusion reactions and will request washed red cells (washing performed by Canadian Blood Services) for patients with recurrent transfusion reactions.

Exchange transfusion: Use AS-3 RBCs, plasma-depleted, matched for Rh and Kell groupings (others if possible), sickle test negative; hematocrit about 0.75, may be reconstituted to a Hct of about 0.5 if desired.

The rationale for these choices includes the following.

- All red cell units are prestorage leukoreduced by Canadian Blood Services, reducing the incidence of febrile transfusion reactions due to white cells or cytokines. Plasma-depletion minimizes transfusion reactions caused by proteins and decreases the volume needed for transfusion. Washing by an automated cell-washer (by CBS) further removes plasma proteins for patients who cannot tolerate the small amounts of residual plasma in plasma-depleted red cells..
- Red cells stored in additive solutions such as AS-3 are well preserved, so “fresh” blood is no longer necessary (AS-3 red cells have a shelf-life of 42 days).
- Phenotypically matched blood minimizes the chance of alloimmunization.
- HbAS (sickle cell trait) blood may be used for simple transfusions (except in severe hypoxic conditions), but should be avoided in exchange transfusions. The Blood Transfusion Laboratory does a sickedox test on all red cell units intended for transfusion into sickle cell anaemia patients, only sickle screen units will be used for exchange transfusions (not simple transfusions).

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Peri-operative Management Guidelines for In-patient Management of Children with Sickle Cell Disease

Background

Children with sickle haemoglobinopathies are predisposed to complications requiring surgical procedures, such as cholecystectomy and splenectomy. These children may also require surgery for the problems that would be encountered in any population. With improvements in intra-operative monitoring and more awareness of the conditions that induce erythrocyte sickling (hypoxia, hypothermia, acidosis, and dehydration), dramatic reductions in perioperative complications have occurred. Despite this, a significant percentage (7%) of all deaths among patients with sickle cell disease are still related to surgery (Platt et al. 1994).

It has been assumed that correction of anaemia and reduction in the percentage of sickle haemoglobin (by simple or exchange transfusion) will prevent intra-operative and post-operative morbidity and mortality in sickle cell patients. The extent of the operative procedure, including post-operative dysfunction and pain, must be assessed and a decision made as to the benefits of pre-operative transfusion therapy.

A retrospective review by Griffin and Buchanan (1993) showed that for the majority of minor elective procedures (hernia repair, circumcision, tympanostomy tube placement, strabismus surgery, and dental rehabilitation) in sickle cell patients, pre-operative transfusions are unnecessary, as these patients usually have uncomplicated courses. On the other hand, patients undergoing thoracotomy, laparotomy, or tonsillectomy/adenoidectomy (T/A) are at higher risk of developing post-operative complications (the rate is 50%) and may benefit from pre-operative transfusion regimens. These procedures are characterized by longer intra-operative duration and by compromised chest wall and pulmonary mechanics.

If transfusion is undertaken, the choice includes simple or exchange (automated or manual) transfusion. A simple transfusion may be of benefit when the patient's haemoglobin is below baseline. But by raising Hb without significantly lowering HbS, a simple transfusion may dramatically increase blood viscosity and thereby increase the risk of sickle-related complications. Partial exchange transfusion allows dilution of HbS without increasing hematocrit. In a multicentre randomized prospective study (Vichinsky et al., 1995) comparing a conservative (simple transfusion) to an aggressive (exchange) transfusion regimen in preventing perioperative complications in patients with sickle cell anaemia, the conservative approach was found to be as effective, and with only half as many transfusion-associated complications (eg: alloimmunization). In addition, transfused (conservative and aggressive) patients undergoing cholecystectomy in this study were compared to a non-transfused sickle population undergoing cholecystectomy. Although the incidence of specific sickle-cell events was higher in the non-transfused cohort, overall morbidity (including that due to transfusion-associated complications) was unaffected by pre-operative transfusion.

In conclusion, it appears reasonable to transfuse pre-operatively patients who are seriously ill, haematologically compromised (Hb 15g/L < baseline), or undergoing major surgeries (thoracotomy, extensive open laparotomy). Patients with a history of pulmonary disease or of frequent recurrent painful crises requiring hospitalization appear to be at a higher risk of complications, and hence should also be transfused. Patients who are in their usual state of health, at baseline Hb, likely do not need a pre-operative transfusion for relatively simple surgeries (cholecystectomy, splenectomy).

Guidelines

1. Examine the patient thoroughly immediately before the operation, to assure that the child is in good health and without any current acute illnesses. If the child is not in his/her usual state of health, the procedure should be postponed. Consider transfusion strongly for children:
 - a) undergoing major procedures—thoracotomy, laparotomy, T/A
 - b) who are ill and in whom surgery cannot be postponed
 - c) with haemoglobin 15g/L below baseline levels
 - d) with significant history of pulmonary disease, stroke, etc.

These issues must be discussed in consultation with a Haematology fellow.

2. All patients should be admitted on the day prior to operation and given IV fluids for a minimum of 12 h at maintenance flow rate. Request Haematology and Anaesthesia consults about issues of management.
3. For anaesthetic management, the room should be pre-warmed, with assurance that temperature can be well monitored and properly maintained, because hypothermia can trigger sickling. The patient should be well oxygenated pre-operatively; induction and intubation should be undertaken with little or no hypoxic insult. Monitor O₂ saturation and ABG closely. Avoid use of tourniquets.

Post-operative Management

Post-op care for patients with sickle cell disease must emphasize pulmonary toilet and avoidance of hypoxia, hypotension, acidosis, and stasis.

1. This begins in the operating room, with assurance that the patient does not become hypothermic, hypoxic, or hypotensive during emergence from anaesthesia. Before extubation, the patient should be well awake, ventilating and oxygenating well.
2. In the recovery ward, assess the patient carefully before transferring the child to a paediatric ward. Request a chest x-ray, if there is any concern about respiratory function.
3. Patients should be monitored for O₂ saturation (aim to keep O₂ sat >96%); children 4 years or older should be on a pulmonary clearing program (incentive spirometry). If atelectasis or oxygen desaturation develops, seriously consider admission to the CCU with intensified efforts at pulmonary clearing, including re-intubation if necessary.
4. Maintain hydration to prevent vasoconstriction, hypoperfusion, and microvascular occlusion, which ultimately lead to sickling. Avoid over-hydration, however, because pulmonary interstitial edema can lead to hypoxia and a sickling crisis.
5. Provide appropriate analgesia so that the patient is co-operative with ambulation and pulmonary clearing, but not so much that he/she is constantly narcotized and asleep.
6. If operative complications develop or the patient becomes toxic or septic, consider early transfer to the CCU (in consultation with Haematology).

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Acknowledgments

These guidelines were prepared with the assistance of Editorial Services, The Hospital for Sick Children, Toronto. The authors thank the following individuals for providing constructive feedback and guidance in the development of these protocols:

David Chiu, MD	Peter Kim, MD
Peter Cox, MD	Melanie Kirby, MD
John Doyle, MD	Wendy Lau, MD
Dennis Geary, MD	Nancy Olivieri, MD
Kathryn Griffiths, BSP	Marcia Palmer, RN
Anna Jarvis, MD	Larry Roy, MD
Sheila Jacobson, MD	Sam Shemie, MD
Tony Khoury, MD	

We especially acknowledge Dr. Victor S. Blanchette for spearheading this effort, and for his timely and very constructive feedback.

Glossary of Abbreviations

7B/C	General Paediatrics ward
ABG	arterial blood gas(es)
ACS	acute chest syndrome
alk phos	alkaline phosphatase (blood test)
ALT	almandine aminotransferase (blood test)
APC	activated protein C
aPTT	activated partial thromboplastin time test
ASSC	acute splenic sequestration crisis
AST	aspartate aminotransferase (blood test)
bid	twice a day (bis in die)
BP	blood pressure
CBC	complete blood count
CCU	Critical Care Unit
CNS	central nervous system
CNS-NP	clinical nurse specialist/nurse practitioner
CPNP	certified paediatric nurse practitioner
CT	computed tomography
CVA	cerebrovascular accident (stroke)
diff	differential blood count
ED	emergency department
g	gram(s)
GGT	γ -glutamyltransferase
GnRH	gonadotropin-releasing hormone
h	hour(s)
Hb	haemoglobin (also designating related genotypes HbA, HbAS, HbS, HbS β^0 , HbS β^+ , HbSC, HbSS)
Hct	hematocrit
Hctd	desired hematocrit
Hcti	initial hematocrit
Hctrp	hematocrit of replacement cells
INR	International Normalised Ratio
IV	intravenous
L	litre(s)
LFT	liver function test(s)
MD	medical doctor
mg/kg	milligrams (of medication) per kilogram of patient's body weight
min	minute(s)
mL	millilitre(s) (note that 1mL = 1 cc)
mo	month(s)
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
npo	nil by mouth
NSAID	non-steroidal anti-inflammatory drug(s)
O ₂	sat blood gas test of level of saturated oxygen
PCA	patient-controlled analgesia (a "pain pump")
PCR	polymerase chain reaction test
po	by mouth (per os)
prn	as needed, as circumstances may require (pro re nata)
pt	patient; pt y, patient-year(s)

PTT	partial thromboplastin time
q	every; q1–2h, every 1 to 2 hours
qhs	at every bedtime
RBC	red blood cell(s); erythrocyte count
RN	registered nurse
RUQ	right upper quadrant
s	second(s)
SCT	Sickle Cell Team (RN, CNS-NP, MD, Social Worker)
SickKids	The Hospital for Sick Children, Toronto, Canada
TBV	total blood volume
tid	three times daily (ter in die)
URTI	upper respiratory tract infection
VBG	venous blood gas(es)
VOC	vaso-occlusive crisis
WBC	white blood cell(s); leukocyte count
wk	week(s)
cross & type	blood typing and cross-matching
y	year(s)

Appendix 1

Mild to Moderate Pain, and Pain Scales

A child with mild pain:

- rates his/her pain as 1–3 on a Verbal Report Scale (of 0–10)
- rates his/her pain as 10–30 on the Oucher test
- may not appear uncomfortable, but complains of pain
- may or may not be crying, may have a neutral facial expression, and may be at rest or shifting position in chair

A child with moderate pain:

- rates his/her pain as 4–6 on the Verbal Report Scale (0–10)
- rates his/her pain as 40–60 on the Oucher
- may show facial grimacing, unhappiness, irritability, and a poor appetite
- may (according to the family) have been unable to carry out normal daily activities, or been uninterested in social interaction

A child with severe pain:

- rates his/her pain as > 7 on the Verbal Report Scale (0–10)
- rates his/her pain as > 70 on the Oucher
- show facial grimacing, unhappiness, irritability, and a poor appetite
- is generally crying, very uncomfortable to the point of agony

Pain Scales

The Oucher and Verbal Report Scale are the two self-report tools used across units at SickKids.

Oucher

The Oucher is available in versions for males and females and in multicultural forms (see attached Oucher tests). The child is asked to point to the picture that best shows how he or she feels.

Verbal Report Scale

The person administering this tool says to the patient, “On a scale of 0 to 10, with 0 being ‘no pain’ and 10 being ‘the worst pain ever’, how would you rate your pain?”

Appendix 2

Instruction Sheet for Children with Sickle Cell Disease Discharged from the Emergency Department

1. Please make sure that your child takes the medicine as prescribed.
2. If your child has been prescribed an antibiotic medicine, be sure he/she finishes it all. If your child takes penicillin regularly, then after the prescribed antibiotic is finished, start giving the penicillin again as usual.
3. Your family doctor, your paediatrician, or the Sickle Cell Clinic (416-813-5859 or 416-813-6443) will want to see how your child is doing. If appointments have been made for follow-up, please do not cancel or skip them, even if your child seems well.
4. Take your child to see a doctor right away, or immediately bring your child to the hospital Emergency Room:
 - If your child has a fever of $\geq 38.5^{\circ}\text{C}$ or $\geq 101^{\circ}\text{F}$, taken orally or by ear thermometer.
 - If he/she has difficulty breathing or is breathing fast.
 - If he/she is unusually weak or floppy (lethargic).
 - If he/she is dehydrated; that is, if he/she will not drink, has thrown up more than once or twice, has no tears when he/she cries, or is passing very little urine.
 - If he/she is very cranky and can not be comforted.
 - If he/she is not answering or reacting to you, or he/she looks confused.
 - If he/she is very pale.
 - If the child's spleen is felt to be larger than usual.
 - If he/she has a lot of tummy pain.
 - If his/her cough is getting worse, or if he/she has a new cough.
 - If he/she seems weak or has muscles that do not seem to be working well.
 - If he/she has swelling of the ankles, knees, elbows, wrists, knuckles, or any other joints.
 - If he/she has pain that is getting worse, despite taking pain medicine that you have given as prescribed.
 - If he has a painful erection of the penis (called priapism) lasting more than 2 hours or less than 2 hours if pain cannot be controlled adequately by painkillers at home.

If your child has one of the problems in this list, take him/her to a doctor or to the hospital Emergency Room right away. Do not wait for the SCT to return your call.

5. If your child has been in the Emergency Room and sent home, please call us on the next regular working day to let us know how he/she is feeling. Call 416-813-6443 or 416-813-8376 Monday to Friday, 8:00 am to 5:00 pm, to speak with a member of the SCT.

Instructions reviewed with: _____ Date/Time: _____