Management of Sickle Cell Disease in Children

Practice Guideline

June 2002

Background

Management of Sickle Cell Disease was identified as a priority for clinical practice guideline development by members of the Child Health Network for the Greater Toronto Area during a 2001 consensus forum.

An expert panel[1] was established, the guideline was developed and distributed throughout the membership for input. The final draft was approved by the Coordinating Committee in April 2002. Implementation throughout the Child Health Network will be accomplished through the following process:

1. Network organizations will facilitate a supportive environment for adoption of CHN Practice Guidelines by incorporating the guidelines into their existing guideline process (order sets, intranet availability, etc).
2. Network organizations will identify a "champion" to take the lead in ensuring implementation at the organization.
3. The CHN guideline will proceed through the organizational process for "approval" (MAC, Pharmacy, etc).
4. Education sessions will be provided for staff. CHN will provide a Power Point Presentation for organizational use.
5. CHN will monitor implementation through a variety of methods and report to members (surveys, chart audits, etc).

Introduction

Children with Sickle Cell Disease may present at an emergency department with complications of their condition and may require admission to a paediatric inpatient unit. These guidelines are intended to provide direction for the management of these complications and are not intended to replace long-term management by a Paediatric Haematologist or at a Sickle Cell Disease clinic.

This guideline addresses the three most common conditions that may cause a visit to an emergency department, namely:

1. Acute Painful Episodes (Vaso Occlusive Crisis)
2. Fever (Rule Out Infection)
3. Acute Chest Syndrome (Pneumonia)

[1] Appendix 1 – Members of CHN Expert Panel for Sickle Cell Disease in Children

General Recommendations

Emergency Triage

- Children presenting at the Emergency Department should be classified as Level 2 (P-CTAS), indicating that they should be assessed by a physician (preferably a paediatrician) within 15 minutes of arrival.
- Patient-specific clinical information should be kept in the emergency department of the hospital(s) frequented by children with Sickle Cell Disease in order to allow staff timely access to relevant history and treatment data.

Hospital Admission

- Children requiring inpatient care should be admitted to a Regional Children's Health Centre.

Surgery

- All surgery for any child with Sickle Cell Disease should be performed at the Hospital for Sick Children.

Consultation with HSC

- The attending physician should consult with a member of the HSC sickle Cell Team or a Haematology Fellow whenever the conditions outlined in Table 1 are present:

Table 1 Conditions Requiring Consultation with HSC

Conditions Requiring Consultation with HSC
• Presence of severe chest syndrome • Positive blood culture result • Clinical condition is deteriorating • Blood transfusion is indicated • Uncertain diagnosis i.e. sickle cell crisis vs. osteomyelitis

Acute Painful Episode (Vaso Occlusive Disease) Management

A vaso-occlusive crisis (VOC) is the most frequent complication of Sickle Cell Disease. It is a condition whereby obstruction of blood flow by sickled erythrocytes leads to hypoxia and acidosis and eventually, to ischemic tissue injury. VOC varies in intensity and duration between patients and between different episodes in the same patient. Precipitating factors may be infection, fever, acidosis, hypoxia, dehydration, sleep apnea, and exposure to extremes of heat and cold. Often, no cause is identified.

Clinical/Laboratory Features

Table 2 outlines the presenting signs relative to the site of the VOC. It also outlines conditions that may mimic VOC as well as conditions that may occur concurrently with VOC.

Table 2 Site and Presenting Signs of VOC

Site of Pain	Signs/Symptoms	Conditions with Similar Presentations	Possible Concurrent Conditions
Bone (extremities, dactylitis, hand/foot, back)	• pain • swelling • low-grade fever • redness • warmth	• osteomyelitis • fracture	• CNS event (stroke) • priaprism • aplastic crisis • fever/sepsis • acute chest syndrome • acute sequestration crisis
Abdomen	• mild to severe abdominal pain	• splenic sequestration • liver sequestration • appendicitis • cholecystitis • urinary tract infection • pelvic inflammatory disease • pneumonia (acute chest crisis)	

Emergency Department Management

1. Obtain a complete history including previous episodes (type, duration, treatment).
2. Perform a physical exam including vital signs, cardiopulmonary and hydration status, spleen size, neurologic exam, presence of jaundice and localizing signs of infection.
3. Conduct the following laboratory tests:[2]

- CBC, differential, reticulocyte count
- Blood type and cross (if in severe pain, Hgb < 15g/L, evidence of bone marrow suppression)
- Urinalysis (if indicated)
- LFTs +/- amylase (if abdominal pain and clinical indications)
- Chest Xray (if chest pain, fever or respiratory symptoms
- Oxygen saturation via pulse oximeter
- Arterial blood gases (if signs of respiratory failure are present)

4. Encourage the patient to drink.
5. Insert an IV (if febrile, dehydrated or in moderate to severe pain)
6. For **mild to moderate pain** give:
    - Acetaminophen (15 mg/kg/dose, maximum dose 65 mg/kg/day,) with codeine (1 mg/kg/dose, maximum dose 60 mg/dose and 6 mg/kg/day) PO Q4H PRN. These can be given separately or together.
    - If pain relief is adequate and there are no other acute complications, the child can be discharged on oral analgesics.
7. For **moderate to severe pain** (or if pain relief as given above for mild to moderate pain is inadequate after 30-60 minutes), give an IV bolus of:
    - Morphine 0.1-0.15 mg/kg/dose (maximum 7.5 mg/dose).
    - Repeat morphine once after 60 minutes if pain relief inadequate.
    - Administer a 10 ml/kg bolus of saline IV, followed by 1.5 times the maintenance fluid requirement of 2/3-1/3 IV (dextrose 3.3% in sodium chloride 0.3% solution).
8. For **severe pain**:
    - Continuous morphine at 40 micrograms/kg/hour.

[2] Kress et al. Chest 1999;115:1316-1320 – Found that pulse oximetry more closely follows co-oximwtry than does calculated oxygen saturation reported with arterial blood gases, during sickle chest syndrome.

9. Additional boluses of morphine 0.05 mg/kg can be given Q 1-2 h PRN.
10. If adequate pain relief is established for 2 hours with 1 or 2 doses of intermittent morphine, consider administering acetaminophen with codeine, as above. Discharge home can follow, if able to take oral analgesics.
11. If more than 2 doses of morphine are necessary, the child should be admitted to hospital.

Outpatient Management

Children should be discharged on oral analgesics:

- Acetaminophen (15 mg/kg/dose) with Codeine (1 mg/kg/dose) PO q4h for a period of 48 hours (acetaminophen max. 65 mg/kg/day, and codeine max. 60 mg/dose and 6 mg/kg/day).
- If pain persists after 48 hours, patients should be re-evaluated.

Inpatient Management

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

Patients should be admitted to the paediatric inpatient unit at a Regional Children's Health Centre.

Analgesia[3]

- Continue morphine at 40 micrograms/kg/hour
- Titrate the dose by 20 micrograms/kg/hour **Q8h** to a maximum of 100 micrograms/kg/hour, **if necessary**, to achieve pain relief
- Boluses of morphine 0.05 mg/kg can be administered Q1-2h PRN for breakthrough pain
- When adequate pain relief is maintained for 24 hours, decrease the dose in 20 microgram/kg/hour decrements Q8h
- Long acting oral morphine (equivalent dose) may be used as an alternative to continuous IV morphine in stable patients

For a pain crisis lasting more than 24-48 hours in a child older than 6 years of age; consider a PCA (patient-controlled analgesia) pump.

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[3] Jacobson SJ, Kopecky EA, Joshi P, Babul N. Randomised trial of oral morphine for painful episodes of sickle-cell disease in children. Lancet 1977; 350: 1358-1361.

Monitoring Guidelines for Patients Receiving Opioid Medication

Children receiving morphine must be carefully monitored for signs of opioid toxicity: hypotension, bradycardia, drowsiness, coma, pinpoint pupils, cold clammy skin, and hypoventilation.

The following guidelines must be followed for patients receiving opioid medications:

Analgesia	Observation/Vital Signs/ Pain Score/Sedation Scale	Oxygen Saturation Monitoring	Resp./ Apnea Monitoring	ECG Monitoring
Continuous Opioid Infusion **Sedation Scale:** **0 None - Alert** **1 Mild - Occasionally drowsy, easy to arouse** **2 Mod - Frequently drowsy, easy to arouse** **3 Severe - Somnolent, difficult to arouse** **S Sleep - Normal sleep, easy to arouse**	***Baseline Assessment*** ▪ Pain assessment, HR, BP, RR, and level of consciousness (LOC) using sedation scale and pain assessment tool prior to administration of the infusion and **q1h for the first 4 hours** of the infusion. ▪ Repeat assessments **q1h for 4 hours after any change** in drug dose or change in infusion rate. ▪ Continuous O2 saturation monitoring throughout the duration of the infusion. ▪ **RR, Sedation Scale q1h**. ▪ **HR, BP, Pain Score**, **q2-4h**.	yes	as ordered	no
Intermittent Opioid Dose	***Baseline Assessment*** ▪ RR, HR, BP, O2 Sat, Sedation Score Then: ▪ RR, HR, BP, Sedation Score **q 5 minutes x 4** - the last time include a Pain Score as well; Then: ▪ q 30 minutes x 2 Then: ▪ as per patient condition/other pre-existing orders **IV Additive (to run over 15 – 20 minutes)** ▪ RR, HR, BP, Sedation Score q10 minutes x 2 Then: ▪ At completion of the flush include a Pain Score Then: ▪ Q30 minutes x 2 Then: As patient condition/other pre-existing orders	• continuous monitoring for patients whose underlying condition predisposes them to respiratory depression	as ordered	no

Additional Inpatient Treatment Recommendations

1. Stool softener (e.g. docusate sodium 5 mg/kg/day) divided into 3 doses unless child has diarrhea
2. Antihistamines for pruritis PRN
3. Hydration: Continue IV/PO fluids at 1-1½ times the maintenance rate
4. Oxygen as necessary to treat hypoxemia (oxygen saturation <94-95%)
5. Incentive spirometry for older children with chest or back pain: 10 breaths Q1-2 h when awake or 5 breaths Q15min.
6. Monitor VS Q4h, fluid intake and output, and daily weight
7. Monitor pain using a developmentally appropriate Pain Tool Q4h, and before and after each pain medication and non-pharmacologic intervention (heating pads, warm baths, other comfort measures such as imagery and distraction)
8. Encourage ambulation and activity as tolerated
9. For unmanageable pain and/or complications result, consult the Sickle Cell Team at HSC and consider transfer
10. If the child is comfortable and has graduated to demand dosing only, switch to oral analgesics:
    - Acetaminophen (10-15 mg/kg/dose) with codeine (1 mg/kg/dose) tablet PO q4h PRN (acetaminophen max. 65 mg/kg/day, and codeine max. 60 mg/dose and 6 mg/kg/day) given separately or together

Discharge Criteria

The child may be discharged if the following criteria are met:

- Taking and tolerating fluids and medication by mouth
- Pain is controlled adequately with PO medications
- Concurrent problems are resolved

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Fever (Rule Out Infection)

Background

By 3-4 months of age (when fetal hemoglobin declines to < 50% of total), many children with sickle cell anemia (HbSS) and sickle b-thalassemia develop clinically significant hemolytic anemia and impairment of splenic function. In others, although the Hb F 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 years 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%.

Therefore, management of children with Sickle Cell Disease should include:

- Early diagnosis and referral to a comprehensive care program for sickle cell disease
- Prophylactic penicillin continued until at least 5 years of age
- If allergy (to penicillin) exists, trimethoprim-sulfamethoxazole may be used
- Vaccination with the polyvalent (23-vaalent) pneumococcal vaccine (0.5 ml SC or IM) and quadrivalent meningococccal vaccine (0.5 ml SC) at 24 months of age
- Vaccination with Haemophilis influenzae type B vaccine (0.5 ml IM)

Despite these measures, septicemia may still occur. Whenever a child with sickle cell disease has an oral temperature of >38.5ºC, he or she should be seen urgently.

Emergency Department Management

1. Place the child in a room immediately, take a history, do a physical exam assessing vital signs, degree of pallor, spleen size, and any neurological deficits, jaundice, or respiratory distress

2. Perform the following laboratory/diagnostic tests tests:

- CBC, reticulocyte count
- Blood culture

3. Start an IV and inject cephtriaxone 80 mg/kg/dose (maximum 2 gm/dose). Cephtriaxone should be given within 30 minutes of presentation and before test results are available; IM injection may be used if IV access is unavailable. Parenteral antibiotics should be given even if there is an obvious focus of infection e.g. otitis media, URTI, etc.
4. If allergy exists to beta-lactam antibiotics, IV clindamycin (40 mg/kg/day, divided Q6-8h, maximum 2.7 gm/day, can be used. Clindamycin should not be used alone in the treatment of suspected meningitis, as it does not cross the blood/brain barrier.
5. If the child is seriously ill, add Vancomycin 60 mg/kg/day, divided Q6h, maximum 4 gm/day.
6. Give acetaminophen (15 mg/kg/dose, Q4h, PRN, maximum 65 mg/kg/day).
7. Additional investigations may be indicated only if there is clinical suspicion of other physical findings:

- Chest Xray, if cough, hypoxemia, chest pain, or fever >40ºC are present
- Oxygen saturation
- Arterial blood gases
- Urine culture
- Lumbar puncture
- Blood type and cross match if pallor, respiratory or neurological symptoms, or splenic enlargement are present
- Throat culture & Stool culture
- Mycoplasma PCR from throat swab and Mycoplasma serology
- 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.

Inpatient Management

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°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 X 10^9/L, Hb < 60 g/L, or platelets < 150 X 10^9/L
- 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)

1. Give IV cefotaxime (200 mg/kg/day, divided q6-8h; max. 8 g/day) until cultures are sterile and clinical status improves (minimum of 48 h).
2. Patients with significant allergy to beta-lactam antibiotics are to be treated with IV Clindamycin (40 mg/kg/day, divided q6-8h; max. 2.7 g/day). Clindamycin is not to be used in the treatment of meningitis, as it does not cross the blood-brain barrier.
3. In children 5 years of age or older with respiratory symptoms, administer erythromycin estolate (40 mg/kg/day IV divided q6h, max. 4 g/day, or, PO divided q6-12h, max. 2 g/day IV).
4. In children younger than 5 y of age, IV erythromycin estolate may be given if high suspicion of Mycoplasma.

Empiric Therapy of Presumed Pneumococcal Meningitis

1. Ceftriaxone (80 mg/kg/dose, q12h x 3 doses then q24h, max. 2 g/dose) plus Vancomycin (60 mg/kg/day divided q6h, max. 4 g/day)
2. For significant allergy to beta lactam antibiotics use Vancomycin (60 mg/kg/day IV, divided q6h, max. 4 g/day) plus Rifampin (20 mg/kg/day PO, divided q12h, max. 1.2 g/day).

Additional Treatment when Child is Critically Ill

1. Give Vancomycin (60 mg/kg/day, divided q6h; max. 4 g/day) to patients who are severely ill (septic), in whom meningitis is suspected, or who deteriorate on cefotaxime/ceftriaxone.

2. Decisions to stop Vancomycin should be made in consultation with Sickle Cell Team at HSC.

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

Additional Inpatient Treatment Recommendations

1. Observe patients closely for any deterioration in clinical status, which may indicate septicemia or development of chest crisis.
2. Measure vital signs q4h.
3. Measure O2 saturation continuously if the patient's O2 sat < 94%, or intermittently
4. Administer O2 to keep oxygen saturation at >94%
5. Administer IV fluids at 1½ times maintenance for the first day (and while patients are afebrile); then reduce to maintenance levels
6. Request blood cultures and CBC daily, if fever persists
7. Request reticulocyte counts every Monday and Thursday
8. If the patient has penicillin/cephalosporin-resistant pneumococcal meningitis, or is not improving after 36-48 h of therapy, do a repeat lumbar puncture as an in vivo measure of treatment effectiveness
9. If the microbiology laboratory reports the 48h cultures as negative, stop antibiotics unless there is a focal infection
10. If the culture is positive and the organism is penicillin-susceptible, change to penicillin (250,000 units/kg/day, divided q4-6h, max. 20 x 106 units/day)
11. If the culture is positive for penicillin-non-susceptible pneumococcus, ensure that the patient is on Vancomycin, in addition to ceftriaxone/cefotaxime and consult with SCT at HSC
12. When patient is ready for discharge, ensure adequate follow-up is in place

Discharge Criteria

The child may be discharged if the following criteria are met:

- Taking and tolerating fluids and medications by mouth
- Afebrile for at least 24 hours, with negative cultures at 48 hours
- Pulmonary symptoms, if any, have resolved

Outpatient Management

Options for Outpatient Management

Outpatient management of sickle cell patients with fever is an area that is still being evaluated. A number of studies[4] have reported the successful use of an outpatient approach in managing a selected group of well-appearing children with fever.

Two general approaches have been utilized in outpatient management. Following the initial dose of ceftriaxone, outpatients 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.

Outpatient 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.

Recommendations for Outpatient Management

Once the decision has been made for outpatient management, a short period of observation in the emergency department (2 – 4 hours) is recommended,

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[4] Rogers ZR, Morrison RA, Vedro DA, et al. Outpatient management of febrile illness in infants and young children with sickle cell anaemia. J Pediatr 1990; 117 (5): 736-739 [a retrospective review of sickle cell patients with fever managed with IV ceftriaxone followed by 3 d of PO Ceclor (cefaclor)].

Wilimas JA, Flynn PM, Harris SC, et al. A randomized study of outpatient treatment with ceftriaxone for selected febrile children with sickle cell disease. N Engl J Med 1993; 329 (7): 472-476 [a randomized study of children with sickle cell disease and fever at low risk for sepsis treated with two doses of IV ceftriaxone q24h vs. inpatient management].

Williams LL, Wilimas JA, Harris SC, et al. Outpatient therapy with ceftriaxone and oral cefixime for selected febrile children with sickle cell disease. J Pediatr Hematol Oncology 1996; 18 (3): 257-261 [a prospective, non-randomized study on use of IV ceftriaxone followed by PO cefixime for febrile sickle cell patients at low risk for sepsis].

followed by re-evaluation prior to discharge (assessment of vital signs, level of consciousness and ability to take fluids and oral medications).

The following criteria should be met when outpatient management is considered:

Criteria for Outpatient Management

1. The child's temperature is < 40°C
2. Recent doses of prophylactic penicillin have not been missed
3. The child is over the age of 1 year
4. WBCs are between 5 and 20 X 109/L; platelets >100 X 10/L
5. There is no systemic toxicity and no other sickle cell complications
6. The patient has no respiratory distress
7. The child has received a dose of ceftriaxone
8. The family has a prescription for an oral antibiotic and there is no physician concern about the family's ability to obtain the medication
9. Follow-up can be ensured. Make note of patient and family compliance with therapy, the family's psychosocial status (is there tremendous upheaval in the family?), etc.
10. Verify that the telephone number available for the family is correct
11. Make sure the family receives an Instruction Sheet
12. The patient should be given a prescription for a 3-day supply of oral antibiotic. We suggest either of the following:
    - cefixime (Suprax®: 8 mg/kg/day, once daily, max. 400 mg/day)
    - cefaclor (Ceclor®: 40 mg/kg/day, divided TID; max. 1.5 g/day)
13. Acceptable alternatives include:
    - cefprozil (Cefzil®)
        - patients 6 mo to 12 years of age: 30 mg/kg/day, divided BID, max. 1 g/day
        - patients >12 years of age: 250-500 mg BID
    - cefuroxime axetil (Ceftin®) 250 mg BID in tablet form (tablets and suspension are not bioequivalent and suspension is very bitter)
    - clarithromycin (Biaxin®) 15 mg/kg/day, divided BID; max. 1 g/day
    - clindamycin 30 mg/kg/day, divided q6-8h (max 2g/day)
14. Patients with significant allergy to beta-lactam antibiotics may be treated with clarithromycin or clindamycin
15. 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 penicillin prophylaxis.

Prior to discharge, verify that adequate follow up has been arranged with the HSC Clinic, if appropriate, or with the child's primary care physician. Parents are to be given an instruction sheet and advised to resume penicillin prophylaxis when the antibiotic is completed.

Follow-up

1. The Paediatrician shall inform the child's primary care physician that the patient was seen in ED, and of the patient's status.
2. The next morning an update on the patient's status should be done by telephone. This call should be made by the child's primary care paediatrician or the paediatrician on call, or by the child's family physician (in consultation with a Paediatrician).
3. In addition, the physician should follow-up on day 3 following discharge, to ensure that there is compliance with medications and that the patient is well.
4. The physician shall also check blood culture results.

Note: Caution is recommended in managing sickle cell patients with fever as outpatients. It is suggested 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 Management

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. Table 1 outlines the most common causes of ACS.

Table 1 Usual Causes of Acute Chest Syndrome

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

In patients with sickle cell disease, ACS occurs most frequently in patients with hemoglobin genotype SS (12.8 events/100 patient-years); less so in those with HbSB0-thalassemia (9.4 events/100 patient-years) or HbSC (5.2 events/100 patient- years); and least often in those with HbSB+-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

Age	Clinical Signs	Seasonal Variation
< 4 years	• Fever • Cough • Upper lobe disease	Winter for all ages
Older children and adults	• Shortness of breath • Chills • Severe pain • No fever • Multi lobe and lower lobe disease	
All ages	• Tenderness over ribs or sternum • Infiltrates in one or more lobes on Xray (66% one lobe only)/ or chest Xray may look normal in first 2-3 days • Pleural effusion in 30% • Decreased Hgb • Increased leukocytes	

Emergency Department Management

1. If fever ≥38.5ºC or if in respiratory distress place immediately in a room and assess
2. If no fever and no breathing difficulties, assess as soon as possible (within 15 minutes, P-CTAS Level 2)
3. Obtain a 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
4. Assess vital signs, cardiopulmonary and hydration status, spleen size, neurologic exam, presence of jaundice, and signs of infection
5. Perform the following laboratory/monitoring tests:
    - CBC, diff, and reticulocyte count
    - Blood culture, if the child is febrile
    - Oxygen saturation monitoring if he or she is in moderate to severe respiratory distress
    - Blood type and cross-matching (for possible exchange transfusion), if in respiratory distress
    - Nasopharyngeal swab
    - Chest Xray and oxygen saturation if fever, chest pain, tachypnea, or respiratory symptoms are present
6. Initiate IV therapy at maintenance rate

7. Administer oxygen to keep saturation above 94-95%
8. Administer IV cefotaxime 200 mg/kg/day, divided Q6-8h; maximum dose 8 gm/day. May follow 24 hours after an initial dose of ceftriaxone in the emergency department
9. Maintain appropriate hydration, analgesic and antipyretic therapy, in addition to other necessary investigations and treatment as per other protocols

Inpatient Management

Note: All patients with ACS should be admitted to the paediatric inpatient unit at a Regional Children's Health Centre or transferred to HSC depending on the severity of the child's condition.

1. Administer hydration, analgesics, and antipyretics as necessary.
2. Continue IV and PO fluids at maintenance flow rates. Increase fluids as needed, if the child is dehydrated or insensible losses are increased (e.g., 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®) 0.5-1 mg/kg/dose, max. 60 mg/dose.
4. If the child has a history of reactive airway disease or wheezing, consider bronchodilators, e.g. salbutamol (Ventolin®).
5. **Antibiotic Therapy**
    - For the first 72 hours of admission, the patient should receive a third-generation cephalosporin (IV cefotaxime, 200 mg/kg/day, divided q6-8h, max. 8 g/day starting 24 hr after the initial admission dose of ceftriaxone)
    - Beyond 72 h, some may be switched to cefuroxime (75 mg/kg/day, divided q8h, max. 4.5 g/day), as follows:
        1. Mild pneumonia & stable: Cefotaxime for 72 h, then cefuroxime
        2. Moderately severe pneumonia: Continue cefotaxime
        3. Severe pneumonia or unstable: Transfer to HSC and provide Cefotaxime + vancomycin 60 mg/kg/day, divided q6h; max. 4g/day
    - Children > 5 years of age should be suspected of having mycoplasma pneumonia; add erythromycin (40 mg/kg/day, IV, divided q6h; max. 4 g/day or PO, divided q6-12h, max. 2 g/day). Use IV erythromycin in patients younger than 5 only if there is evidence of mycoplasma

- Patients with a significant beta-lactam antibiotic allergy can be treated with clindamycin (40 mg/kg/day, IV/PO, divided q6h; max. 2.7 g/day); or 30 mg/kg/day PO divided q6-8h (Max 2gm/day)

6. 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, i.e. during every set of television commercials
7. Encourage ambulation and activity. The hospital's Child Life representative can recommend structured daily activity
8. Request a CBC daily during the hospital stay; and arterial/venous blood gases (ABG/VBG) daily, if not improving, Consider transfusion according to the following guidelines:

Transfusion guidelines:

1. Contact the HSC Haematology consult fellow and consider transfer to HSC
2. Patients with mild to moderate disease and hemoglobin (Hb) at baseline do not generally need a transfusion
3. Patients with moderately severe disease and Hb 15 g/L less than baseline should be transfused with packed RBCs, 10 mL/kg (simple transfusion)
4. Patients should not be transfused to a Hb of greater than 100 g/L (Hct > 30%)

9. Patients with severe disease-extensive infiltrates; worsening ABGs; increasing need for oxygen (> 40% O2) and decreasing oxygen saturation; need for CCU; etc. require an exchange transfusion (RBC cytapheresis). Transfer immediately to HSC.
10. When ready for discharge, ensure adequate follow-up.

Discharge Criteria

The child may be discharged if the following criteria are met:

- The child does not require supplemental oxygen
- The patient has been afebrile for at least 24 hours
- The child is taking fluids and medications by mouth
- Pain control is adequate with PO medications
- Concurrent problems are resolved

Note: The role of steroids (four doses of IV dexamethasone: 0.3 mg/kg/dose, q12h) in preventing clinical deterioration and reducing the need for transfusions is unclear (unpublished data from George R. Buchanan, Dallas, Texas) and requires further study.

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APPENDIX 1

Expert Panel on Sickle Cell Disease for Children

Members

Dr. Jeremy Friedman	Paediatrician, HSC
Dr. Robert Lau	Paediatric Haematologist, WOHC
Dr. Steven Comay	Paediatric Haematologist, NYGH
Yvette Dalrymple	Paediatric Nurse Educator, RVHS
Marcie Palmer	RN, Sickle Cell Clinic, HSC
Mary Paulin	North York CCAC