**Definition:** Sickle cell disease is an inherited red blood cell disorder that can cause both acute and chronic complications and is used to refer to the many genotypes that cause the characteristic clinical syndrome. (1)

**Pathophysiology:** Sickle cell anemia (otherwise known as HbSS, or homozygous B^{+} allele) is the most common form, with the second most prevalent type being HbSC, or HbSβthalassemia. (1) The genetic mutation that causes sickle cell disease creates an HbS polymerization that can disrupt hemoglobin architecture and flexibility and oxidative cellular stress. (1) The mutation can result in the processes of vaso-occlusion with ischemia and reperfusion injury and hemolytic anemia. (1)

**Epidemiology:** It is estimated that sickle cell disease affects approximately 100,000 Americans in the United States, and occurs in 1 of every 365 Black or African American births, and 1 of every 16,300 Hispanic-American births. Approximately 1 in 13 African-American babies is born with sickle-cell trait. With the utilization of pneumococcal vaccines and hydroxyurea therapy, the mortality rate for sickle cell disease has been dramatically reduced. (2)

**Etiology:** Vaso-occlusion crises (VOCs) are thought to be caused by microvascular obstruction and tissue ischemia (ischemia-reperfusion injury) and hemolytic anemia. (1) Although VOCs commonly occur in the extremities, when they occur in other sites they may be confused with, or can be in the early stages of, other acute complications, and etiology of the pain must be determined in order to rule out potential causes other than uncomplicated VOC. (3) Other acute complications that can manifest in acute vaso-occlusive pain include stroke, acute chest syndrome, renal infarction, myocardial infarction, priapism, splenic or hepatic sequestration, or stroke/transient ischemic attack. (3)

Acute chest syndrome (ACS) is both a common and serious complication of sickle cell disease. Symptoms of lower respiratory tract disease can present suddenly and be accompanied by a new pulmonary infiltrate on chest x-ray, although these changes may be subtle in the early stages. (3) The most common well-defined etiology is viral or bacterial infection (particularly *Mycoplasma pneumoniae*), but the complication may also result from bone marrow fat embolism, intrapulmonary aggregates of sickled cells, atelectasis, or pulmonary edema. (3)

**Inclusion Criteria**
- Patients 1-21 years with sickle cell disease

**Exclusion Criteria**
- Children <1 year
- Patients without sickle cell disease
- Patients who exhibit signs of stroke

### Diagnostic Evaluation

**History: Assess for**
- Lower respiratory symptoms (cough, wheezing, tachypnea, chest pain) and/or
- Previous history of acute chest syndrome episode, asthma, or stroke/transient ischemic attack
- Vaccination status

**Physical Examination**
- Assessment for the possibility of other serious complications concurrently with the treatment of pain
- Assess for abnormal vital signs, particularly changes in respiratory rate (RR), use of accessory muscles, color
- Auscultate lungs
- Assess for pain associated with abdominal distension for signs of shock (See Table 2 and 3)
- Obtain pulse oximetry; detect new onset hypoxemia
- Rate severity of SCD according to Clinical Respiratory Score (CRS) (See Table 1)
- Evaluate for signs and symptoms of shock (See Table 2 and 3)

### Table 1. Clinical Respiratory Score

<table>
<thead>
<tr>
<th>Assess</th>
<th>Clinical Respiratory Score (CRS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score 0</td>
</tr>
<tr>
<td><strong>Respiratory Rate</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;2 mos: &lt;50</td>
<td>&lt;2 mos: 50-60</td>
</tr>
<tr>
<td>2-12 mos: &lt;40</td>
<td>2-12 mos: 40-50</td>
</tr>
<tr>
<td>1-5 yrs: &lt;30</td>
<td>1-5 yrs: 30-40</td>
</tr>
<tr>
<td>&gt;5 yrs: &lt;20</td>
<td>&gt;5 yrs: 20-30</td>
</tr>
<tr>
<td><strong>Auscultation</strong></td>
<td></td>
</tr>
<tr>
<td>Good air movement,</td>
<td></td>
</tr>
<tr>
<td>scattered expiratory</td>
<td></td>
</tr>
<tr>
<td>wheezing, loose</td>
<td></td>
</tr>
<tr>
<td>rales/crackles</td>
<td></td>
</tr>
<tr>
<td>Depressed air movement,</td>
<td></td>
</tr>
<tr>
<td>inspiratory and</td>
<td></td>
</tr>
<tr>
<td>expiratory wheezes or</td>
<td></td>
</tr>
<tr>
<td>rales/crackles</td>
<td></td>
</tr>
<tr>
<td>Diminished or absent</td>
<td></td>
</tr>
<tr>
<td>breath sounds, severe</td>
<td></td>
</tr>
<tr>
<td>wheezing, or rales/crackles, or marked prolonged expiration</td>
<td></td>
</tr>
<tr>
<td><strong>Use of Accessory Muscles</strong></td>
<td></td>
</tr>
<tr>
<td>Mild to no use of</td>
<td></td>
</tr>
<tr>
<td>accessory muscles, mild</td>
<td></td>
</tr>
<tr>
<td>to no retractions, no</td>
<td></td>
</tr>
<tr>
<td>nasal flaring on</td>
<td></td>
</tr>
<tr>
<td>inspiration</td>
<td></td>
</tr>
<tr>
<td>Moderate intercostal</td>
<td></td>
</tr>
<tr>
<td>retraction, mild to</td>
<td></td>
</tr>
<tr>
<td>moderate use of</td>
<td></td>
</tr>
<tr>
<td>accessory muscles, nasal</td>
<td></td>
</tr>
<tr>
<td>flaring</td>
<td></td>
</tr>
<tr>
<td>Severe intercostal and</td>
<td></td>
</tr>
<tr>
<td>substernal retractions,</td>
<td></td>
</tr>
<tr>
<td>nasal flaring</td>
<td></td>
</tr>
<tr>
<td><strong>Mental Status</strong></td>
<td></td>
</tr>
<tr>
<td>Normal to mildly irritable, agitated, restless.</td>
<td>Lethargic</td>
</tr>
<tr>
<td>Room Air SpO₂</td>
<td>90%-95%</td>
</tr>
<tr>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Normal to normal</td>
</tr>
</tbody>
</table>

(Add score from all rows to calculate total CRS score)
Table 2. PALS Adjusted Vital Signs for Septic Shock

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart Rate</th>
<th>Resp Rate</th>
<th>Systolic BP</th>
<th>Temp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0d - 1m</td>
<td>&gt;205</td>
<td>&gt;60</td>
<td>&lt;60</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt;1m - 3m</td>
<td>&gt;205</td>
<td>&gt;60</td>
<td>&lt;70</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt;3m - 1y</td>
<td>&gt;190</td>
<td>&gt;60</td>
<td>&lt;70</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt;1y - 2y</td>
<td>&gt;190</td>
<td>&gt;40</td>
<td>&lt;70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt;2y - 4y</td>
<td>&gt;140</td>
<td>&gt;40</td>
<td>&lt;70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt;4y - 6y</td>
<td>&gt;140</td>
<td>&gt;34</td>
<td>&lt;70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt;6y - 10y</td>
<td>&gt;140</td>
<td>&gt;30</td>
<td>&lt;70 + (age in yr x 2)</td>
<td>&lt;36 or &gt;38.5</td>
</tr>
<tr>
<td>&gt;10y - 13y</td>
<td>&gt;100</td>
<td>&gt;30</td>
<td>&lt;90</td>
<td>&lt;36 or &gt;38</td>
</tr>
<tr>
<td>&gt;13y</td>
<td>&gt;100</td>
<td>&gt;16</td>
<td>&lt;90</td>
<td>&lt;36 or &gt;38</td>
</tr>
</tbody>
</table>

Table 3. Signs and Symptoms of Shock

<table>
<thead>
<tr>
<th>Exam Abnormalities</th>
<th>Cold Shock</th>
<th>Warm Shock</th>
<th>Non-Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Pulses</td>
<td>Decreased</td>
<td>Bounding</td>
<td></td>
</tr>
<tr>
<td>Capillary Refill (central vs. peripheral)</td>
<td>≥3 sec</td>
<td>Flash (&lt;1 sec)</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Mottled, cool</td>
<td>Flushed, ruddy, erythroderma (other than face)</td>
<td>Petechiae below the nipple, any purpura</td>
</tr>
<tr>
<td>Mental Status</td>
<td>Decreased, irritability, confusion, inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Laboratory Tests:
- Obtain a complete blood count with reticulocyte count and note changes in baseline CBC or reticulocyte count or any laboratory abnormalities (such as increasing creatinine, liver function tests, coagulation abnormalities, etc.).

Critical Points of Evidence*

Evidence Supports
- Collect complete blood count with differential, platelet count, reticulocyte count initially and daily for the patient with acute chest syndrome until the patient is improving. Results should be compared to the patient’s baseline values. (4-7) – Strong recommendation, low quality evidence
- Collect secretory phospholipase A2 (sPLA2) levels for the suspicion of acute chest syndrome when the lab becomes available at Texas Children’s Hospital. (7) – Strong recommendation, low quality evidence
- Obtain a chest radiograph if patient has cough, chest pain, hypoxemia, or lower respiratory symptoms at presentation to the hospital or during admission. Fever in the absence of these symptoms does not necessitate evaluation with a chest radiograph. (8-12) – Strong recommendation, very low quality evidence
- Encourage oral fluid intake and to administer total fluid intake (intravenous plus oral) at maintenance rate to encourage that the patient remains euolemic. (13) – Strong recommendation, very low quality evidence
- Transfuse the patient with acute chest syndrome with PRBCs to a hemoglobin goal of 9-10 g/dL. (14,15) – Strong recommendation, very low quality evidence
- Use continuous pulse oximetry monitoring in patients with sickle cell disease who experiencing vaso-occlusive crisis who are being treated in the emergency center. (16-22) – Strong recommendation, very low quality evidence
- Encourage incentive spirometry in patients with sickle cell disease at risk for or with acute chest syndrome who are admitted to the hospital. (23-26) – Strong recommendation, low quality evidence
- Administer inhaled bronchodilators every 6 six to eight hours with acute illness if patient has a history of asthma or presents with wheezing. (23-26) – Strong recommendation, very low quality evidence
- Administer a one week course of prednisolone or three days of dexamethasone to patients who have clinical wheezing with or without a known history of asthma who are being treated in the inpatient setting. (27-31) – Strong recommendation, very low quality evidence
- Administer ketorolac in patients with mild to moderate pain. (32-34) – Strong recommendation, very low quality evidence
- Administer ketorolac as adjuvant therapy while initiating morphine via patient controlled analgesia for patients with severe pain (pain scores greater than seven). (32-34) – Strong recommendation, very low quality evidence
• Administer intranasal fentanyl or oral morphine for pain control in patients when there is a delay in IV placement. (35-38) – Strong recommendation, low quality evidence
• Try any non-pharmacologic intervention to help control pain. (39-44) – Strong recommendation, low quality evidence
• Use a high basal dose with a low on demand (intermittent opioid infusion) morphine via patient controlled analgesia in patients who present with pain crisis. Titrate depending on patient’s pain control as determined by patient self-report of pain score. Once patient has achieved good control, wean until patients intravenous opioid dose can be transitioned to an oral dose. (45-49) – Strong recommendation, low quality evidence

Evidence Against
• Avoid corticosteroids unless indicated. (27-31) – Strong recommendation, very low quality evidence

Evidence Lacking/Inconclusive
• Progress to intrapulmonary percussive ventilation (IPV) or vest therapy if patient appears to be worsening. – Strong consensus recommendation
• Use of a risk score to predict health care utilization – Unable to make a recommendation
• Using functional pain scales as compared to traditional pain scales to assess pain in children – Unable to make a recommendation
• Administer antibiotics of symptoms suggest acute chest or if the patient has worsening respiratory distress. – Strong consensus recommendation

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

Consults/Referrals:
• Consult Pulmonary Service prior to discharge for CRS ≥5
• Consult Critical Care Medicine for CRS ≥4
• Consider Pain Service consult for: child hospitalized ≥3 days with no clinical improvement, avascular necrosis, unmanageable side effects from PCA, failure to control pain after titrating up and trying other agents, or complicated pain history
• Consider Child Life request to see for coping concerns and/or procedural preparations

Discharge Criteria:
• Improved pulmonary symptoms and documentation of adequate oxygenation on room air
• Afebrile ≥24 hours and negative cultures for ≥24-48 hours, if applicable
• Stable hemoglobin/hematocrit
• Taking adequate oral fluids and able to take PO medications, if applicable
• Adequate pain relief with oral analgesics, if applicable
• Slow wean from steroids (over 7-10 days), if applicable
• Home care agencies notified as needed

Caregiver understands:
• Discharge care, including steroid wean, if applicable
• When Hematology Clinic and Pulmonary SCD Clinic follow-ups scheduled
• How and when to use IS
• Medications and how to obtain them

Measures
Structure
• Availability of sPLA2 laboratory testing

Process
• Order set utilization in the EC and inpatient units
• Documentation of CRS scores every 4 hours
• Incidence of pulmonary treatments
• Length of time on oxygen
• Frequency of ambulation
• Time to PCA initiation
• Percentage of patients with CRS ≥5 referred to pulmonary clinic
• Percentage of patients/caregivers who received IS and IS education
• CRS score of patients transferred to PCU/PICU
• Percentage of patients with documented RT consult upon arrival to unit

Outcome
• Number of patients who develop ACS
• Number of simple blood transfusions
• Number of exchange transfusions
• Number of patients transferred to the PCU or PICU
• ED and IP LOS
• Time on opioid
• Total PCA morphine dose
• Number of patients with ACS with identified pathogen
• Number of patients with unscheduled return visit to the ED/triage and/or admission for the same diagnosis within 14 days of discharge
Texas Children’s Hospital Evidence-Based Outcomes Center

Sickle Cell Disease Respiratory Management Algorithm

DATE: July 2017

**Texas Children’s Hospital Evidence-Based Outcomes Center**

**Sickle Cell Disease Respiratory Management Algorithm**

**Clinical Respiratory Score (CRS)**

- **Assess CRS every 4 hours**
- **Does the patient meet ACS Criteria?**
- **Yes**
  - Initiate ceftriaxone injection: 50 mg/kg IV for 30 min (MAX: 2 g/day)
  - If signs of fluid overload, consider furosemide 0.5 mg/kg IV X 1 dose (MAX: 40 mg/dose)
  - If pt is allergic to penicillin/cephalosporin, substitute clindamycin: 10 mg/kg/dose IV q 6-8 h (MAX: 900 mg/dose)
- **No**
  - Assess CRS and manage patient based on score

**CRS < 2**
- Vital signs q 4 h
  - Continuous pulse oximetry (goal SpO2 of 95% unless ACS is suspected)
  - Transfer to Hb goal of 9-10 g/dL

**CRS 2-3**
- Vital signs q 2 h
  - Continuous pulse oximetry (goal SpO2 of 95% unless ACS is suspected)
  - Transfer to Hb goal of 9-10 g/dL
  - If pt is < 5 years:
    - Vest TID if pt is 10 kg
    - Vest or IPV TID (best preferred if wheezing)

**CRS 4**
- Consider transfer to PCU or PICU (consider management in PICU if history of previous ACS or exchange transfusion)
- Consult Pulmonary Service prior to discharge
- Continuous pulse oximetry (goal SpO2, unless ACS is suspected)
- Transfer to Hb goal of 9-10 g/dL
- Consider exchange transfusion to 10 g/dL
- Manage in PCU
  - Continuous pulse oximetry (goal SpO2), unless ACS is suspected
  - Consult Pulmonary Service prior to DC
  - Perform exchange transfusion (NOTE: Remove venous catheters as soon as possible after exchange transfusion)
  - BIPAP + IPV q 4 h (may use vest instead of IPV if wheezing)

**CRS 5**
- If wheezing or rales/crackles:
  - Methylprednisolone: 1 mg/kg/dose IV q 6 h (MAX: 80 mg/dAY)
- Manage in PICU
  - Continuous pulse oximetry (goal SpO2), unless ACS is suspected
  - Consult Pulmonary Service

**CRS ≥ 6**
- If fever, give ceftriaxone injection: 50 mg/kg IV for 30 min (MAX: 2 g/day)
- If signs of fluid overload, consider furosemide 0.5 mg/kg IV X 1 dose (MAX: 40 mg/dose)
- If pt is allergic to penicillin/cephalosporin, substitute clindamycin: 10 mg/kg/dose IV q 6-8 h (MAX: 900 mg/dose)
- If Pt is allergic to penicillin/cephalosporin, substitute clindamycin: 10 mg/kg/dose IV q 6-8 h (MAX: 900 mg/dose)
- Administer azithromycin: 10 mg/kg PO on day 1 (MAX: 500 mg/dose), then 5 mg/kg PO once daily (MAX: 250 mg/dose) for 4 days (erythromycin may be substituted)
- If severe illness, consider adding vancomycin: for children < 70 kg: 15 mg/kg/dose IV q 8 h; for children ≥ 70 kg: 1 gram IV q 12 h (MAX: 1 gram/dose)
- If signs of fluid overload, consider furosemide 0.5 mg/kg IV X 1 dose (MAX: 40 mg/dose)
- IV fluids should be given at no more than maintenance
- Repeat CXR if signs and symptoms are worsening

Follow-up considerations

For more severe cases of Acute Chest Syndrome, make follow-up appointment in joint Heme/Pulm clinic.

July 2017

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**Pain Management Algorithm for Patients With Sickle Cell Disease in Vaso-Occlusive Crisis**

**Child with sickle cell disease presents with persistent pain**
(Notify Hematology Clinic or Hematology Fellow on call after initial assessment)

**Mild pain (score 1-3)**
- NS bolus followed by 1 ½ x maintenance, unless ACS is suspected
- Apply warm packs to painful areas
- Depending on severity of pain, if patient on home opioids, escalate 15-25% of home medication equivalent
- Morphine 0.1 – 0.2 mg/kg/dose (MAX: 8 mg) IV
- Ketorolac 1 mg/kg for first dose, then 0.5 mg/kg every 6 h not to exceed 5 days (MAX: 30 mg/dose)
  (NOTE: avoid use of ketorolac in pts w/ renal dysfunction, ARF, ESRD, or Scr > 2 x baseline, or active bleeding)
- Assess pain 30 min after administration of ketorolac

**Patient pain moderate to severe?**

**Moderate/Severe pain (score 4-10)**
- NS bolus followed by 1 ½ x maintenance, unless ACS is suspected
- Apply warm packs to painful areas
- Depending on severity of pain, if patient on home opioids, escalate 15-25% of home medication equivalent
- Morphine 0.1 – 0.2 mg/kg/dose (MAX: 8 mg) IV
- Ketorolac 1 mg/kg for first dose, then 0.5 mg/kg every 6 h not to exceed 5 days (MAX: 30 mg/dose)
  (NOTE: avoid use of ketorolac in pts w/ renal dysfunction, ARF, ESRD, or Scr > 2 x baseline, or active bleeding)
- Assess pain 30 min after administration of ketorolac

**Patient received total of 3 doses morphine?**
- Repeat morphine 0.1 – 0.2 mg/kg/dose IV q 10 min (MAX: 8 mg)

**Pain well controlled?**

**Pain well controlled?**
- Oral fluids
- Apply warm packs to painful areas
- Give oral morphine (0.2-0.5 mg/kg; MAX: 30 MG Q4 hours)
- Give ibuprofen (if none within last 6 hours)

**Observe for 1 h in ED**

**Pain remains well controlled?**
- Discharge on oral morphine (0.2-0.5 mg/kg) (alternate w/ ibuprofen)
- Emphasize fluid intake
- Give SCD discharge instruction sheet
- Instruct patient to follow up in clinic in 3-5 days

**Patient pain moderate to severe?**

**Observe for 20 min - 1 h in ED**

**Pain remains well controlled?**
- Discharge on oral morphine (0.2-0.5 mg/kg) (alternate w/ ibuprofen)
- Emphasize fluid intake
- Give SCD discharge instruction sheet
- Instruct patient to follow up in clinic in 3-5 days

**Admit**
- Notify PCP

**NOTE:**
- If pt asleep after administering pain meds, wake patient up to reassess pain as directed. (e.g., q 10 min x 3)
- If patient is unable to tolerate morphine, use dilaudid IV/PCA at standard 1:10 conversion
- If pain ≥ 4 and unable to access IV within 15 minutes, consider administering oral morphine or intranasal fentanyl

**NOTE:**
- Administer IV antibiotics if the patient is ill-appearing, toxic-appearing, febrile, or has a significantly elevated white count. Refer to the septic shock guideline if suspicion of shock. Be cautious with fluid management if concern for acute chest syndrome.

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DATE: July 2017
NOTE: If child on home opioids, give
- morphine, use
- dilaudid IV/PCA at standard 1:10
- conversion

- If patient is unable to tolerate
- morphine, use
- dilaudid IV/PCA at standard 1:10
- conversion

NOTE: Replace ketorolac w/ oral ibuprofen after 5 days, if needed

Instructions for opioid weaning:
- If pt's PCA demands are ≤¼ of actual dose available, consider switching pt to oral meds (long-acting for basal, short-acting for bolus)
- If pt's condition improving and FLACC score has improved ≥ 2 measurements over 2 shifts, titrate down from continuous to long-acting
- Assess need for PCA every 24 h

NOTE: Avoid use in pts w/ renal dysfunction, ARF, ESRD, or SCr > 2 x baseline, or active bleeding

NOTE: If child on opioids, give
- ibuprofen after 5 days, if needed

NOTE: Administer IV antibiotics if pt is febrile, toxic-appearing, septic, or has a significantly elevated white count. Refer to the sepsis shock guidelines if suspicion of shock. Be cautious with fluid management if concerned for acute chest syndrome, especially with dehydrations.

Sickle Cell Disease in Vaso-Occlusive Crisis Inpatient Pain Management Algorithm

Child w/ SCD presents with persistent pain; consider nonpharmacologic methods to complement medication

Pain remains well controlled?

Yes

Pain remains well controlled?

Yes

Consider Oral or PCA morphine

Oral morphine: 0.2 to 0.5 mg/kg Q 3-4 hours

Initiate morphine PCA:
- Loading dose (mg/kg) – 0.1
- Basal rate (mg/kg/h) – 0.02
- Intermittent dose (mg/kg) – 0.035
- Lockout interval (min) – 10

IV fluids 1.5 x maintenance, unless ACS is suspected

Initiate bowel regimen (long-acting for basal, short-acting for bolus)

Begin DC planning for opioid weaning

Begin DC planning “see below for instructions on opioid weaning

Consult Pain Service

NOTE: IVFs + PO intake should equal:
- 1.5 x maintenance, unless ACS is suspected
- 2 x baseline, or active bleeding

NOTE: Rebalance opioid dose every 4-6 h.

Instructions for opioid weaning:
- If pt's PCA demands are ≤¼ of actual dose available, consider switching pt to oral meds (long-acting for basal, short-acting for bolus)
- If pt's condition improving and FLACC score has improved ≥ 2 measurements over 2 shifts, titrate down from continuous to long-acting
- Assess need for PCA every 24 h

Consider consulting Pain Service for:
- child hospitalized ≥ 3 days with significant clinical improvement
- Avascular Necrosis (AVN)
- unmanageable side effects from PCA
- failure to control pain after titrating up and trying other agents
- complicated pain history

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References


Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children’s Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts

2. Review of Existing External Guidelines
   - Sickle Cell Disease: Managing acute painful episodes in hospital (National Institute for Clinical Excellence) 2012

3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane Library, CINAHL, Guidelines Clearinghouse, Google Scholar

4. Critically Analyze the Evidence

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- 3 meta-analyses, 15 randomized controlled trials, and 37 nonrandomized studies

5. Summarize the Evidence

- Materials used in the development of the guideline, evidence summary, and order sets are maintained in a Vaso-occlusive Crisis in Sickle Cell Disease evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. The AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

- **Evidence Supports**: Evidence from unbiased random studies or exceptionally strong evidence from observational studies
- **Evidence Against**: Evidence from randomized controlled trials (RCTs) with serious flaws or indirect evidence, or imprecise results) or unusually strong evidence from biased observational studies
- **Evidence Lacking/Inconclusive**: Evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<table>
<thead>
<tr>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High</strong></td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td><strong>Low</strong></td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td><strong>Very Low</strong></td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
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Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of vaso-occlusive crisis in children with sickle cell disease. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards
(guidelines, summaries, or pathways) do not set out the standard of care, and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient family, to make the ultimate judgment regarding care.

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jun 2011</td>
<td>Originally completed</td>
<td></td>
</tr>
<tr>
<td>Jul 2017</td>
<td>Updated</td>
<td></td>
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