# Sickle Cell Disease: Stroke
# Clinical Pathway Synopsis

## Sickle Cell Disease: Stroke – ED/Inpatient Algorithm

**Inclusion criteria:**
- Child diagnosed with sickle cell disease (SCD) presenting with signs/symptoms of a suspected stroke

*Note. If child is known to CMKC, review the Critical Information note and type of SCD (HbSS and HbSβ$^0$ thalassemia have a higher risk of stroke than HbSC or HbSβ+)*

**History**
- Stroke, transient ischemic attack
- Headaches
- Nausea or vomiting
- Visual changes
- Weakness
- Loss of coordination
- Numbness and tingling
- Fever
- Syncope
- Seizures
- Recreational or prescribed drug use

**Physical Exam**
- Baseline mental status with detailed neurologic exam
- Hydration status
- Signs of infection

**Differential Diagnosis**
- Complicated migraine
- Posterior reversible encephalopathy syndrome
- Seizure
- Cerebral venous sinus thrombosis, refer to *Cerebral Venous Sinus Thrombosis Clinical Pathway*
- Hemorrhagic stroke
- Meningitis
- Sepsis, refer to *Sepsis Clinical Pathway*
- Vaso-occlusive crisis, refer to *Sickle Cell Disease: Management of Acute Pain Clinical Pathway*

*This list is not all inclusive of possible differential diagnoses*

**Acute Sickle Cell Stroke Neuroprotective Care**
- Head of bed flat, if tolerated and there are no signs of increased intracranial pressure
- Avoid hypotension: Bolus as needed with NS 10 - 20 mL/kg
- Normovolemia: NS at maintenance ***-or-*** D5NS if glucose < 100
- Saturations > 96%
- Normothermia: Treat temperature > 38°C with antipyretics, with or without cooling blanket
- Seizure control:
  - As soon as able with any suspected seizure activity
  - Consider continuous EEG to monitor subclinical seizures (*consult Neurology as soon as able for seizure prophylaxis recommendations*)

Child with sickle cell presents with signs/symptoms of a suspected stroke (ED/Inpatient)
***Activation of Stroke Alert is not indicated***

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**History and Physical**
- Obtain history and complete physical exam
- Consider differential diagnosis

**Immediate Stabilization Management**
*(Use EDP Sickle Cell Stroke [Suspected]or Sickle Cell Stroke [Suspected] Powerplan)*

If patient presents to CMK ED, plan to immediately transfer to Adele Hall for imaging/transfusion as soon as possible after initial stabilization, IV placement, and labs

- **Provide supplemental oxygen:** Maintain oxygen saturation levels above 96%
- **Monitor vital signs:** Check vital signs, including blood pressure, every 15 minutes for the first hour
- **Provide neuroprotective care**
- **NPO status and IV access**: Keep the child NPO (nothing by mouth) and establish IV access
- **Pain management:** Ensure adequate pain control
- **Prepare for PICU admission:** Notify the PICU early for admission and potential RBC exchange
- **Consultations**: (1) Contact PICU and consult Hematology/Oncology early to help guide evaluation process and treatment; (2) Involve Apheresis Team; and (3) Consult Neurology if seizures present or if presentation unclear or not entirely consistent with stroke
- **Order MRI:** Use Stroke protocol imaging embedded in order set
- **Place Blood Bank and laboratory tests orders:**
  - **Blood Bank**: Type and cross-match for sickle-negative PRBCs (*order 1 unit for child < 30 kg and 1 - 2 units for child > 30 kg*), hold blood as per blood bank for extended phenotype
  - **Laboratory tests**: CBC with differential, reticulocyte count, hemoglobin S, BMP, Mg, iCa, Phos, PT, INR, aPTT, LFT, fibrinogen, D-Dimer, urine hCG (*for female > 10 years of age*) or serum beta hCG, POC glucose
- **Fever management**: If child has a fever,
  - Obtain blood culture then treat with acetaminophen and antibiotics
    - Consider administering ceftriaxone +/- azithromycin, if concerns for acute chest

**Do not delay treatment while waiting for imaging, notification from consulting providers, or while placing orders to obtain labs or get IV access - *quickly transferring to the PICU to initiate definitive treatment is encouraged, particularly if high suspicion for sickle cell stroke***

**Imaging and Transfusion**
- If Hgb < 8.5 g/dL, initiate transfusion of 15 mL/kg PRBCs over 2 hours
- Obtain MRI if it can be done safely ***-and-*** within 60 minutes
  - If MRI is **NOT** available within 60 minutes, obtain non-contrast head CT STAT
- If uncertain of diagnosis, request stat MRI while waiting for requested Hgb SS fraction
  - Full MRI is preferred given the broader differential
  - Encourage discussion between attending (PICU) and attending radiologist

***Transfusion should not delay imaging***

Does imaging identify hemorrhage, ischemic stroke, or inconclusive findings?

- Hemorrhage → • Consult Neurosurgery • Plan for PICU admission
- Ischemic Stroke → Admit to PICU and prepare for exchange transfusion once in PICU
- Inconclusive → Admit to PICU ***-or-*** Hematology service if child is stable

*These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare a clinical pathway for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.*

## Sickle Cell Disease: Stroke – PICU/Inpatient Algorithm

Neurocritical Care: Sickle Cell Stroke Summary

**Pheresis Catheter Recommendations**
- May refer to Children's Mercy *Partial Manual Packed Red Blood Cell Exchange* policy for venous access options and decision-making
- **If port present, contact Apheresis Team regarding its use for exchange**
- **Femoral line suggestions**:
  - < 15 kg: 8 Fr
  - 15 - 30 kg: 10 Fr
  - > 30 kg: 12 Fr
- **Internal jugular line suggestions:**
  - < 20 kg: 8 Fr
  - 20 - 50 kg: 10 Fr
  - > 50 kg: 12 Fr

***Notes.***
- Children < 5 kg require manual red cell exchange. Call Hematology for recommendations
- Children > 15 kg are eligible for automated exchange
- Children 5 - 15 kg will require additional blood to prime apheresis machine and require further discussion with Apheresis Team

**Acute Sickle Cell Stroke Neuroprotective Care**
- Head of bed flat, if tolerated and there are no signs of increased intracranial pressure
- Avoid hypotension: Bolus as needed with NS 10 - 20 mL/kg
- Normovolemia: NS at maintenance ***-or-*** D5NS if glucose < 100
- Saturations > 96%
- Normothermia: Treat temperature > 38°C with antipyretics, with or without cooling blanket
- Seizure control:
  - As soon as able with any suspected seizure activity
  - Consider continuous EEG to monitor subclinical seizures (*consult Neurology as soon as able for seizure prophylaxis recommendations*)

**Discharge Criteria**
- Clinically and neurologically stable ≥ 24 - 36 hours post transfusion(s)
- Afebrile for at least 24 hours
- Able to take fluids and medications orally

Child admitted to PICU for exchange transfusion due to sickle cell stroke

**Treatment**
- Use Sickle Cell Stroke (Suspected) admission order set
- Continue IV fluids at 1x maintenance flow rates (*total fluid intake should **NOT** exceed maintenance*)
- Provide adequate pain control
- Place pheresis catheter
- Ensure Hematology/Oncology, Neurology, and Apheresis Team consults in place

*Avoid hyperosmolar therapies which may worsen sickling*

**Prior to Exchange**
- Provide neuroprotective care
- Ensure pre-exchange transfusion labs were obtained prior to exchange
- Call Blood Bank to request cross-matching multiple units in preparation for exchange transfusion
- Call lab to confirm receipt of Hgb S (*do not wait for Hgb S level to initiate apheresis*)

**For Imaging-Confirmed Sickle Cell Stroke or Suspected Based on History and Physical**
- If Hgb < 5, advise simple transfusion only
- If Hgb 5 - 8.5, perform RBC exchange transfusion to a Hgb of 9 - 12 and Hb S goal of 15 - 20% of total Hgb. Perform simple transfusion if delay in exchange is expected
- If Hgb > 8.5, perform RBC exchange transfusion to a Hgb of 9 - 12 and Hb S goal of 15 - 20% of total Hgb

**Upon Completion of Exchange Transfusion**
- Obtain BMP, iCa, Mg, Phos, Hgb S (*batch pre- and post- apheresis Hgb S labs*)
- If appropriate (Hgb S < 30%), consider removal of the central venous catheter to reduce the risk of thrombosis

**Additional ICU/Inpatient Management**
- Encourage ambulation and activity
- Consult Rehab Medicine, Psychology, Speech Therapy, Physical Therapy, Occupational Therapy
- Consult Neurosurgery if child has evidence of Moyamoya Syndrome and/or concerns with steno occlusive disease on initial MRI/MRA

**Prior to Discharge**
Inform Sickle Cell Team in order to organize clinic follow-up and schedule next transfusion

**Discharge**
- Validate follow-up arrangements have been made with Sickle Cell Team, Neurology, Physical Therapy, Rehab Medicine, and Apheresis if ongoing automated exchanges are indicated
- Validate follow-up arrangements have been made with Neurosurgery (*if patient has evidence of Moyamoya*)

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**Objective of Clinical Pathway**

To provide care standards for children, adolescents, or adults diagnosed with sickle cell disease experiencing signs or symptoms of a suspected stroke. The Sickle Cell Disease: Stroke Clinical Pathway guides the early identification and management when presenting to the emergency department or experiencing symptoms during an inpatient stay through hospital discharge.

**Background/Epidemiology**

Children with sickle cell disease (SCD) have an increased risk of experiencing a cerebral infarct or stroke (DeBaun et al., 2020; Parikh et al., 2023). Approximately 40% of these children will experience an asymptomatic or silent stroke by the age of 18 years (DeBaun et al., 2020; Parikh et al., 2023). Regardless of whether the stroke is symptomatic or silent, the child can sustain lasting neurological sequelae or death, rendering early identification and management imperative (DeBaun et al., 2020; Parikh et al., 2023).

The Sickle Cell Disease: Stroke Clinical Pathway Committee sought to align the clinical pathway with the American Society of Hematology (ASH) guidelines (DeBaun et al., 2020), published after the initial version of the pathway was released in 2018. Expressly, parameters are provided regarding the timing and type of transfusion for children presenting with acute neurological symptoms. Prompt blood transfusion is the recommended treatment for suspected or confirmed ischemic stroke or transient ischemic attack (DeBaun et al., 2020). Furthermore, the Sickle Cell Disease: Stroke Clinical Pathway Committee aims to ensure early identification and notification to the multi-specialty team involved in the immediate stabilization and management of a child, adolescent, or adult with sickle cell disease when a stroke is suspected.

**Target Users**

- Physicians (Emergency Medicine, Hospital Medicine, Intensivists, Fellows, Residents)
- Nurse Practitioners
- Nurses

**Target Population**

***Inclusion Criteria***

- Child diagnosed with sickle cell disease, presenting with signs and symptoms of suspected stroke.

*Note.* If the child is known to Children's Mercy Kansas City, review the Critical Information note and type of SCD (*HbSS and HbSβ$^0$ thalassemia have a higher risk of stroke than HbSC or HbSβ+*)

**AGREE II**

Two national guidelines provided guidance to the Sickle Cell Disease: Stroke Clinical Pathway Committee (DeBaun et al., 2020; National Heart, Lung, and Blood Institute, 2014). See Table 1 and Table 2 for AGREE II.

Table 1

*AGREE II Summary for the American Society of Hematology 2020 Guidelines for Sickle Cell Disease: Prevention, Diagnosis, and Treatment of Cerebrovascular Disease in Children and Adults (DeBaun et al., 2020)*

| Domain | Percent Agreement | Percent Justification^ |
|---|---|---|
| Scope and purpose | 80% | The aim of the guideline, the clinical questions posed and target populations **were** identified. |
| Stakeholder involvement | 97% | The guideline **was developed** by the appropriate stakeholders and represents the views of its intended users. |
| Rigor of development | 88% | The process used to gather and synthesize the evidence, the methods to formulate the recommendations and to update the guidelines **were** explicitly stated. |
| Clarity and presentation | 100% | The guideline recommendations **are** clear, unambiguous, and easily identified; in addition, different management options are presented. |

| | | |
|---|---|---|
| Applicability | 83% | Barriers and facilitators to implementation, strategies to improve utilization and resource implications **were addressed** in the guideline. |
| Editorial independence | 100% | The recommendations **were not** biased with competing interests. |
| Overall guideline assessment | 91% | |
| See Practice Recommendations | | |

*Note:* Four EBP Scholars completed the AGREE II on this guideline.
^Percentage justification is an interpretation based on the Children's Mercy EBP Department standards.

Table 2
*AGREE II Summary for Evidence-Based Management of Sickle Cell Disease (National Heart, Lung, and Blood Institute, 2014)*

| Domain | Percent Agreement | Percent Justification^ |
|---|---|---|
| Scope and purpose | 84% | The aim of the guideline, the clinical questions posed and target populations **were** identified. |
| Stakeholder involvement | 92% | The guideline **was developed** by the appropriate stakeholders and represents the views of its intended users. |
| Rigor of development | 93% | The process used to gather and synthesize the evidence and the methods to formulate the recommendations **were** explicitly stated. |
| Clarity and presentation | 100% | The guideline recommendations **are** clear, unambiguous, and easily identified; in addition, different management options are presented. |
| Applicability | 82% | Barriers and facilitators to implementation, strategies to improve utilization and resource implications **were addressed** in the guideline. |
| Editorial independence | 83% | The recommendations **were not** biased with competing interests. |
| Overall guideline assessment | 89% | |
| See Practice Recommendations | | |

*Note:* Four EBP Scholars completed the AGREE II on this guideline.
^Percentage justification is an interpretation based on the Children's Mercy EBP Department standards.

**Practice Recommendations**

Please refer to the National Heart, Lung, and Blood Institute (2014) and the American Society of Hematology guidelines (DeBaun et al., 2020) for evaluation and treatment recommendations.

**Additional Questions Posed by the Clinical Pathway Committee**

No clinical questions were posed for this review.

**Updates from Previous Versions of the Clinical Pathway**

- Included differential diagnosis considerations during history and physical examination
- Provided guidance for early notification of multiple specialties during immediate stabilization
- Adjusted normovolemia guidance during immediate stabilization
- Clarified blood transfusion volumes to minimize the delay in initiation
- Updated pheresis catheter recommendations
- Included neuroprotective care recommendations during management while in the Pediatric Intensive Care Unit (PICU)
- Provided parameters for transfusion type and goals

**Recommendation Specific for Children's Mercy**

There were no deviations from the ASH guidelines (DeBaun et al., 2020) regarding practice recommendations, but logistical processes specific to Children's Mercy Kansas City were added.

- Reminder that non-sickle cell stroke activation is not needed
- Guidance for power plan use and early notification of multiple specialties, specifically PICU, Hematology/Oncology, Neurology, Apheresis Team, Blood Bank, and Anesthesia consult during the immediate stabilization and treatment process

**Measures**

- Use of Sickle Cell Disease: Stroke Clinical Pathway
- Use of associated power plans

**Value Implications**

The following improvements may increase value by reducing healthcare costs and non-monetary costs (e.g., missed school/work, loss of wages, stress) for patients and families and reducing costs and resource utilization for healthcare facilities.

- Decreased risk of delayed recognition and management of sickle cell stroke
- Decreased risk of overtreatment (i.e., activation of non-sickle cell stroke alert when sickle cell stroke alert is more appropriate)
- Decreased unwarranted variation in care

**Organizational Barriers and Facilitators**

***Potential Barriers***

- Variability of acceptable level of risk among providers
- Challenges with follow-up faced by some families

***Potential Facilitators***

- Collaborative engagement across care continuum settings during clinical pathway development
- High rate of use of the clinical pathway
- Standardized order set for Emergency Department, Hospital Medicine, and Pediatric Intensive Care

**Power Plans**

- EDP Sickle Cell Stroke (Suspected)
- Sickle Cell Stroke (Suspected)

**Associated Policies**

- Sickle Cell Disease with Fever Standing Order
- Sickle Cell Disease with Pain Standing Order
- Sickle Cell Related Pain

**Education Materials**

- Stroke in the Sickle Cell Patient
  - Found in Cerner depart process
  - Available in English and Spanish

**Clinical Pathway Preparation**

This pathway was prepared by the Evidence Based Practice (EBP) Department in collaboration with the Sickle Cell Disease: Stroke Clinical Pathway Committee composed of content experts at Children's Mercy Kansas City. If a conflict of interest is identified, the conflict will be disclosed next to the committee member's name.

**Sickle Cell Disease: Stroke Clinical Pathway Committee Members and Representation**

- Shabnam Arsiwala, MD, FAAP | Hematology/Oncology/BMT | Committee Co-Chair

- Jay Rilinger, MD | Critical Care Medicine | Committee Co-Chair
- Celeste Tarantino, MD | Pediatric Emergency Medicine | Committee Member
- Marcie Files, MD | Neurology | Committee Member
- Lejla Music Aplenc, MD | Pathology and Laboratory Medicine | Committee Member
- Cherie Scanlon Burroughs, RN, BSN, CPN | Therapeutic Apheresis Services | Committee Member
- Sarah Dierking, MSN, RN, CPHQ | Clinical Practice and Quality | Committee Member
- Jennifer Flint, MD | Critical Care Medicine, Pediatric Critical Care Transport | Contributor

**EBP Committee Members**

- Todd Glenski, MD, MSHA, FASA | Anesthesiology, Evidence Based Practice
- Kelli Ott, OTD, OTR/L | Evidence Based Practice

**Clinical Pathway Development Funding**

The development of this clinical pathway was underwritten by the following departments/divisions: Emergency Medicine, Critical Care Medicine, Hematology/Oncology/BMT, Neurology, Pathology and Laboratory Medicine, Therapeutic Apheresis Services, Clinical Practice and Quality and Evidence Based Practice

**Conflict of Interest**

The contributors to the Sickle Cell Disease: Stroke Clinical Pathway have no conflicts of interest to disclose related to the subject matter or materials discussed.

**Approval Process**

- This pathway was reviewed and approved by the Sickle Cell Disease: Stroke Committee, Content Expert Departments/Divisions, and the EBP Department; after which they were approved by the Medical Executive Committee.
- Pathways are reviewed and updated as necessary every 3 years within the EBP Department at CMKC. Content expert teams are involved with every review and update.

**Review Requested**

| Department/Unit | Date Obtained |
|---|---|
| Pediatric Emergency Medicine | March 2025 |
| Critical Care Medicine | March 2025 |
| Hematology/Oncology/BMT | March 2025 |
| Neurology | February 2025 |
| Therapeutic Apheresis Services | March 2025 |
| Clinical Practice and Quality | February 2025 |
| Pediatric Critical Care Transport | February 2025 |
| Evidence Based Practice | February 2025 |

**Version History**

| Date | Comments |
|---|---|
| August 2018 | Version one – (algorithms developed for ED/Inpatient and PICU/Inpatient, associated powerplans developed) |
| June 2021 | Version two – (algorithms revised) |
| March 2025 | Version three – (ED/Inpatient and PICU/Inpatient algorithms revised, associated powerplans reviewed and updated alert notification distribution list, educational information in Depart reviewed, associated synopsis developed) |

**Date for Next Review**

- March 2028

**Implementation & Follow-Up**

- Once approved, the pathway was presented to appropriate care teams and implemented. Care measurements will be assessed and shared with appropriate care teams to determine if changes need to occur.
- Power plans were updated to include the current alert notification distribution list
- Education was provided to all stakeholders:
  - Nursing units where the Sickle Cell Disease: Stroke Clinical Pathway is used
  - Department of Hematology/Oncology/BMT, Neurology
  - Providers from Emergency Medicine, Critical Care Medicine, Therapeutic Apheresis Services, Pathology and Laboratory Medicine, and Pediatric Critical Care Transport
  - Resident physicians
- Additional institution-wide announcements were made via email, hospital website, and relevant huddles.

**Disclaimer**

When evidence is lacking or inconclusive, options in care are provided in the supporting documents and the power plan(s) that accompany the clinical pathway.

These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time.

It is impossible to anticipate all possible situations that may exist and to prepare clinical pathways for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.

**References**

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Sickle Cell Related Pain, (October, 2022), *CMH Patient Care Services Standards Manual*. Children's Mercy Hospital, Kanas City, Missouri