BOTTOM LINE RECOMMENDATIONS

Sickle Cell Disease

Sickle cell disease (SCD) is a genetic disorder of hemoglobin, in which sickling of red blood cells results in hemolysis and vaso-occlusion. Newborn screening has led to early identification of SCD in many regions across Canada.[1] While homozygous SCD (HbSS) is the most severe, other sickling syndromes (e.g., HbSC) may present similarly. Patients with SCD can present with a number of complications including:

- Fever
- Vaso-Occlusive Episode
- Acute Chest Syndrome
- Aplastic Anemia
- Stroke
- Splenic Sequestration
- Priapism

MANAGEMENT CONSIDERATIONS

Emergent assessment

Starting **pain management within 30-60 minutes** of arrival,[2] and reassessments every 30-60 minutes.[2,3] Febrile patients should be assessed and have **antibiotics started within 30-60 minutes of arrival.**[1]

- New neurologic deficits should be urgently assessed for possible stroke.
- Abdominal pain should be urgently assessed for possible splenic sequestration.
- Priapism is a surgical emergency.

Investigations: For fever or respiratory symptoms: CBC, reticulocyte count, bilirubin (total and direct), and type and screen.[3] All febrile patients also require blood cultures.

- Consider blood gas, urine culture, lumbar puncture, stool culture based on clinical presentation.[3] For infants < 2 months, refer to the AAP Clinical Practice Guidelines for Well Appearing Febrile infants 8-60 Days Old.[4]
- Consider nasopharyngeal swab for respiratory viruses and mycoplasma pneumonia serology for respiratory symptoms.[1]
- Perform chest X-ray for all patients with respiratory symptoms or SpO_2 <95%, and consider in those with isolated fever.

Blood transfusions: The decision to transfuse should be based on both clinical status and context and should be guided in many instances by the baseline hemoglobin. Indications for transfusion may include:[1]

- Acute chest syndrome
- Acute splenic sequestration with severe anemia
- Aplastic anemia with profound drop in reticulocytes
- Isolated severe anemia (Hgb ≥20 g/L below baseline OR <60 g/L if baseline unknown)

FEVER (Temperature ≥ 38ºC oral or ≥38.5 ºC rectal)

Infection is the most common cause of SCD-related mortality. Febrile patients require prompt investigation and intervention.

- Children with SCD who are under/unimmunized, including additional immunizations, and/or not on prophylactic antibiotics are at an even higher risk of serious bacterial infection.[1]
- IV antibiotics should be given. A 2nd or 3rd generation cephalosporin is recommended. Additional antibiotics should be chosen based on the clinical picture, as outlined in Table 1 below.[3]
- Identify signs of sepsis including poor perfusion, hypotension, tachycardia and/or altered mental status and manage appropriately. Refer to TREKK Pediatric Severe Sepsis Algorithm for management.
- Admission and ongoing IV antibiotics are indicated for patients meeting any of the high-risk criteria below. If patient has no high risk criteria AND reliable follow up of blood culture results, discuss admission vs. outpatient management with Pediatrics/Pediatric Hematology/Pediatric Referral Centre.[3] Admit to hospital if blood cultures become positive at any time.

High risk criteria:[3]

- Hemodynamic instability or unwell appearance
- Fever ≥40ºC
- Age <6 months
- Respiratory distress
- Leukopenia (WBC <5x10^9/L), leukocytosis (WBC >30x10^9/L), thrombocytopenia (PLT <100 x10^9/L), or significant anemia (<60g/L or a ≥ 20g/L drop from baseline)
- Severe illness including meningitis, osteomyelitis, acute chest syndrome, splenic sequestration
- Previous history of pneumococcal sepsis and/or meningitis
- Severe pain that cannot be managed at home
- Unable to arrange close follow up

BOTTOM LINE RECOMMENDATIONS

Sickle Cell Disease

VASO-OCCLUSIVE EPISODE (VOE)

Pain is the most common presentation and most frequent cause of admission in SCD.[3] VOE can be triggered by dehydration, illness, fever, surgery, cold exposure, and stress.

» Patients with SCD may not present with typical pain symptoms, even when experiencing severe pain. Consider **splenic sequestration** in all patients with abdominal pain. **Dactylitis** is more commonly seen in infants.[5] Consider other painful conditions in SCD such as osteomyelitis, acute vascular necrosis, acute chest syndrome, stroke, as well as non-SCD related causes of pain.
» For uncomplicated VOE, no investigations are required.
» Treat pain with regularly scheduled NSAIDs and acetaminophen for all patients. For moderate to severe pain, intranasal fentanyl can be given followed immediately by oral morphine.[1] IV morphine should be given if pain is not controlled with intranasal and oral medications. Refer to TREKK Recommendations for Pain Treatment.
» Encourage oral hydration or start IV fluids as required. Apply supplemental oxygen to maintain $SpO_2 \geq 95\%$. Antibiotics are not required if there is no fever or findings suggesting infection.
» Discharge home if pain is well controlled on oral medication, family have access to prescribed medication, and follow up is arranged with a practitioner who manages the child's SCD. If admitting, consult Pediatric Hematology or transfer to Pediatric Referral Center.[2]

ACUTE CHEST SYNDROME (ACS)

ACS is a potentially life-threatening complication of SCD, and a leading cause of morbidity.[3] Diagnostic criteria are:[1,3]

1) **New pulmonary infiltrate** involving ≥1 lung segment (not atelectasis) **AND**
2) **Fever and/or respiratory symptoms** including cough, wheeze, respiratory distress, chest pain

» ACS is more common in children than adults. Children with asthma and SCD are twice as likely to develop ACS as those with SCD alone.[3] Symptoms of ACS overlap with both asthma and lower respiratory tract infections.
» Pulse oximetry should be done routinely for all patients with SCD, and patients with fever or pain crisis should be monitored for early detection of ACS.
» Apply O_2 via mask/nasal prongs to maintain $SpO_2 \geq 95\%$. Consider treating patients with a history of asthma using bronchodilators.[5] Refer to TREKK Pediatric Severe Asthma Algorithm for management.
» Administer IV antibiotics – see Table 1 below.
» Treat pain. Refer to TREKK Recommendations for Pain Treatment. **Avoid over-sedation** and subsequent hypoventilation.
» Maintain hydration with oral and/or IV fluids as needed. **Avoid over-hydration**, and monitor fluid balance.
» Discuss blood transfusion with Pediatrics/Pediatric Hematology/Pediatric Referral Centre. Urgent transfusion may prevent clinical deterioration.
» All patients with ACS should be admitted to Pediatric Referral Centre with ability to provide critical care support and exchange transfusion if the patient deteriorates.

APLASTIC ANEMIA

Many viral illnesses, particularly Parvovirus B19, can cause transient red cell aplasia in SCD resulting in severe acute anemia.[5]

» Symptoms can include fever, pain, fatigue, headache and pallor. Severe reticulocytopenia is seen (reticulocytes <1%).
» Illness is self-limited, lasting 7-10 days. Blood transfusion may be indicated for severe anemia or if symptomatic, and can be discussed with Pediatrics/Pediatric Hematology/Pediatric Referral Center.

STROKE

Stroke is a rare but serious complication and should be investigated for **any new neurologic deficit**. SCD is the most common cause of stroke in children.[3]

» Headache, sudden weakness, abnormal speech, seizures, abnormal gait, and/or any focal neurologic deficit are red flags for stroke, however younger patients may present with only a change in behaviour.[5]
» Urgent CT should be obtained, but if negative with a high suspicion for stroke, an MRI/MRA is indicated.[1]
» For any **suspicion of stroke, arrange urgent consultation with Pediatric Hematology, Pediatric Neurology and transport to Pediatric Referral Centre** with the capacity for exchange transfusion and critical care support.

BOTTOM LINE RECOMMENDATIONS

Sickle Cell Disease

SPLENIC SEQUESTRATION

Splenic sequestration caused by blood trapping in the spleen can lead to hypovolemic shock. It is diagnosed by splenic enlargement and a sudden drop in hemoglobin. Most common between 6 months-5 years but may occur in adolescence.[1] Patients with HbSC are also at high risk at older ages.[5]

» Symptoms include weakness, pallor, tachycardia, tachypnea, left upper quadrant pain and splenomegaly. Atypical symptoms such as back, left flank, and/or chest pain can occur.

» If the spleen is newly enlarged, or larger than baseline, obtain CBC, reticulocyte count, blood type and cross match.[3]

» For any **suspicion of splenic sequestration obtain urgent consultation with Pediatric Hematology and Pediatric Referral Center for potential in-patient management.**

PRIAPISM

Priapism is a prolonged erection unrelated to sexual stimuli. SCD is the most common cause of priapism in children.[5]

» Initial assessment includes time from onset, presence of pain, and precipitating events. Ultrasound with doppler can be done to assess flow but should not delay surgical consult. Supportive care includes IV hydration, analgesia and supplemental O_2 to keep $SpO_2 \geq 95\%$.[5]

» Priapism **≥4 hours** is a surgical emergency, and Pediatric Urology/Urology should be consulted early in course.

» If surgical services are unavailable, aspiration, irrigation, and/or instillation of vasoconstrictive medication into corpora cavernosa should be discussed with a urologist and performed urgently.

Table 1: Antimicrobials for Sepsis and Acute Chest Syndrome (Age >1 month)

Drug	Dose	Indication
Ceftriaxone	100 mg/kg/dose (MAX 2000 mg/dose) IV q24h Meningitic dose: 100 mg/kg/dose (MAX 2000 mg/dose) IV x 1 dose then 12 hours later 50 mg/kg/dose (MAX 2000 mg/dose) IV q12h	Initial antibiotic of choice for sepsis and acute chest syndrome. Includes salmonellae spp coverage if osteomyelitis is suspected.
Clindamycin	40 mg/kg/**day** IV divided q8h (MAX 900 mg/dose)	Alternative to ceftriaxone if beta lactam allergy is suspected.
Vancomycin	15 mg/kg/dose (MAX 1000 mg/dose) IV q6h	Add if MRSA risk factors present, if clinically unwell or for patients with hemodynamic instability.
Azithromycin	10 mg/kg/dose (MAX 500 mg/dose) on Day 1, followed by 5 mg/kg/dose (MAX 250 mg/dose) for remainder of treatment	Add for all patients > 5 years of age with respiratory symptoms. Consider in < 5 years if high suspicion for mycoplasma.
Oseltamivir	< 1 year: 3 mg/kg/dose (MAX 30 mg/dose) PO BID 1 year or older: ≤ 15 kg: 30 mg PO BID >15 – 23 kg: 45 mg PO BID > 23 – 40 kg: 60 mg PO BID > 40 kg: 75 mg PO BID	Consider addition if high suspicion for influenza.

For a full list of references and development team members, please see the following page.

BOTTOM LINE RECOMMENDATIONS

Sickle Cell Disease

Bottom Line Recommendations

Bottom Line Recommendations are short summaries for healthcare providers of the latest knowledge related to the diagnosis and management of pediatric emergency conditions. This resource is not intended to be used as a step-by-step guide. It is ideal for educational purposes and to summarize existing evidence on sickle cell disease exacerbations in pediatric emergency care. Development of this resource involved a rigorous and iterative process, bringing together experts from a variety of specialties (nursing, simulation, emergency medicine, intensive care, and pharmacy). To learn more about the development, see the References & Development Team section below.

References

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To see our resource development process please visit our website here.

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