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STATEMENT OF FINANCIAL DISCLOSURE

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Sickle Cell Emergencies

Sickle cell disease is a very common inherited genetic disorder in the United States, and patients with this disorder frequently present to acute care centers for evaluation and treatment. These patients require expert care to prevent and avert the life-threatening consequences of their disease. Many advances have been made that have improved the life expectancy for patients with this disease and emergency medicine physicians must be aware of these new modalities for diagnosis and treatment to optimize care. This article comprehensively reviews the current standard of care for children with sickle cell disease.

— Ann M. Dietrich, MD, FAAP, FACEP, Editor

Sickle cell disease (SCD) is the most common inherited genetic disorder in the United States, and the population frequency of the HbS allele is increasing.[1] SCD was first described in Chicago in 1910 in a West Indian dental student named Walter Clement Noel. Since then, progress in SCD diagnosis and treatment has improved care for children with SCD. Notable advances include a national newborn screening program, infection prevention with penicillin prophylaxis and vaccines against encapsulated organisms, hydroxyurea to decrease painful crises and possibly ameliorate end-organ injury associated with SCD,[2] chronic red blood cell transfusions to reduce stroke risk, and cure with hematopoietic stem cell transplant (HSCT).[1,3-8] Despite these advances, life expectancy remains in the fifth to sixth decade for those with hemoglobin SS disease.[9-12]

SCD patients depend on urgent and emergent hospital-based care for treatment of the life-threatening consequences of their disease.[13-18] Physicians' attitudes toward these patients leads to differences in pain management and outcomes.[19,20] Recent publications about the care of patients with SCD include the National Institute of Health's updated SCD evidence-based practice guidelines and reviews of emergency care for adult sickle cell patients and atypical presentations in children with SCD.[13,21,22 23] This article will review common emergencies in pediatric SCD.

Classification

Multiple genotypes cause SCD with variable phenotypic expression. Sickle cell anemia refers to the homozygous inheritance of the abnormal hemoglobin sickle (HbS) gene. Table 1 shows ß-globin mutations causing the different clinical phenotypes of SCD.

EXECUTIVE SUMMARY

- Risk factors for developing acute chest syndrome include respiratory infections, treatment with opiates, and splinting due to chest or abdominal pain.
- Thrombocytopenia is uncommon and should alert the physician to the possibility of hepatic or splenic sequestration
- Hydroxyurea is expected to modify hematologic parameters: Hemoglobin may be higher than expected (9-10 g/dL in patients with HbSS) and reticulocyte count low. Macrocytosis is expected. Thrombocytopenia and neutropenia are common side effects and may indicate a supratherapeutic dose.

Table 1. Classification of Sickle Cell Disease

Genotype	Hemoglobin Quantification in %					Phenotype (severity of disease and baseline range of Hb)
	HbA	HbS	HbF	HbC	HbA2	
HbAA (normal)	96	-	2	-	2	Normal
HbAS (trait)	50	45	2	-	2	Normal
HbSS	-	96	2	-	2	Severe, Hb 6-9 g/dL
HbSC	-	48	3	47	2	Moderate severe; stroke much less common. Hb 9-12 g/dL
HbSß$^+$	6	85	5	-	4	Moderate severe, Hb 10-13 g/dL
HbSß^0	-	93	2	-	5	Severe, Hb 6-9 g/dL

Adapted from: Glassberg J. Evidence-based management of sickle cell disease in the emergency department. *Emerg Med Pract* 2011;13:3 and Quinn C T. Sickle cell disease in childhood: From newborn screening through transition to adult medical care. *Pediatr Clin North Am* 2013;60:1363-1381.)

Pathophysiology

Normal adult hemoglobin (HbA) is a tetramer of four proteins, two α- and two ß-globin chains. In SCD, abnormal ß-globin chains called hemoglobin sickle are produced as a result of the substitution of valine for glutamic acid on position 6 of the beta globin gene on chromosome 11. The interactions between mutated ß-chains leads to abnormal protein folding and polymerization, causing red blood cell (RBC) sickling. The severity of sickling depends on the inheritance pattern of the HbS gene (*see Figure 1*). HbS polymerization is exacerbated by changes to temperature, pH, and hydration. Interactions between rigid erythrocyte polymers and the vascular endothelium drives platelet activation and inflammation, causing vascular dysfunction.[24]

Two major pathophysiological processes cause the clinical manifestations of SCD: hemolytic anemia and vaso-occlusion with ischemia-reperfusion (I/R) injury.[25] The serologic consequences of hemolysis are anemia, hyperbilirubinemia, and reticulocytosis. Hemolysis also contributes to vasculopathy that is associated with pulmonary hypertension, renal hyper filtration, chronic leg ulcers, and priapism in SCD. Free plasma Hb causes endothelial damage and depletes nitric oxide, further aggravating vasculopathy.[1] I/R injury causes inflammation and worsens endothelial dysfunction, contributing to vaso-occlusive pain crises. (*See Figure 2*.)

Laboratory Findings

Common laboratory evaluations useful in patients with SCD are described in Table 2. Rapid interpretation of the complete blood count (CBC) and reticulocyte count in patients with SCD helps identify when immediate intervention is required. For each parameter, comparison with patients' baseline guides interpretation.

Hemoglobin: SCD patients have baseline hemoglobin that varies based on genotype. Knowing the patient's genotype and baseline hemoglobin is essential for interpreting the CBC. Many parents know their child's usual "normal" hemoglobin. For children with HbSS, this is usually 7-9 g/dL. A robust reticulocyte count is essential for children with SCD, as sickled RBC's life span is only 7-10 days compared to the 120 days of a typical RBC. Therefore, any child with SCD and a low (uncompensated) reticulocyte count with anemia may develop life-threatening anemia, called an aplastic crisis.

Platelets: Thrombocytosis is common in patients with SCD because of underlying inflammation. Thrombocytopenia is uncommon and should alert the physician to the possibility of hepatic or splenic sequestration.

Leukocytes: Many patients with SCD have a modest leukocytosis at baseline due to chronic inflammation. Marked leukocytosis should always be concerning for infection in

Table 2. Common Studies in Patients with Sickle Cell Disease

Test	Significance
CBC	Anemia is expected; baseline varies and is influenced by genotype and clinical condition; leukocytosis and thrombocytosis are common during inflammatory crises — VOC, ACS, osteomyelitis; thrombocytopenia may indicate hepatic or splenic sequestration. Hydroxyurea may cause pancytopenia.
Reticuloctye Count	Given short t1/2 of sickle cell erythrocytes, patients are dependent on robust reticulocyte production to maintain their hemoglobin. A low reticulocyte count may be found as a harbinger of aplastic crisis or during such crises. Hydroxyurea also suppresses the reticulocyte count.
Liver Function Tests	Indirect hyperbilirubinemia is common. When possible, compare obtained value with historic values. If elevated above baseline, consider hemolytic crisis or cholelithiasis especially if accompanied by direct hyperbilirubinemia. AST is usually modestly elevated due to hemolysis. Hydroxyurea toxicity may cause elevations in AST and ALT.
Hemoglobin Quantitation	Values are reported as a percent and represent the types of hemoglobin present. Interpretation guides genotype diagnosis. The goal of emergent exchange transfusion is to decrease the HbS to at least 30% (equal to the HbS fraction in patients with HbAS.
Blood culture	Aerobic blood cultures should be drawn on any sickle cell patient with fever or in whom a bacterial infection is otherwise suspected.
Chest XR	Indicated for any patient with chest pain, fever or cough. Findings of a new infiltrate makes the diagnosis of acute chest syndrome
Head CT	If MRI is not immediately available or practical, non-contrast head CT should be used as a first line test in patients with headache, seizure or focal weakness in whom stroke is a concern. If negative and ongoing concern, MRI should be obtained.
Diffusion Weighted MRI	The most sensitive and specific study to define cerebrovascular accidents in children with sickle cell disease. Practical considerations may limit their emergent use — young patients may require sedation and technical expertise may be limited after hours.

patients with SCD.

Hemolysis markers: Lactate dehydrogenase, aspartate aminotransferase, unconjugated bilirubin, and reticulocyte count are serological markers of hemolysis and may be elevated at baseline in patients with SCD.

Interpreting the CBC of children treated with hydroxyurea (HU) is increasingly important. HU is expected to modify hematologic parameters: Hemoglobin may be higher than expected (9-10 g/dL in patients with HbSS) and reticulocyte count low. Macrocytosis is expected. Thrombocytopenia and neutropenia are common side effects of HU and may indicate a supratherapeutic dose.[26] At least one case of significant accidental HU ingestion is reported without injury to the child.[27]

Clinical Manifestations of Sickle Cell Emergencies by System: Pulmonary

Acute Chest Syndrome. Acute chest syndrome (ACS) is a clinical diagnosis defined as a new infiltrate on chest X-ray in the presence of fever, cough, tachypnea, or chest pain. Underlying infection and bone infarct with fat emboli likely contribute to the evolution of this life-threatening complication of SCD. ACS may progress rapidly to multi-organ failure and is a leading cause of death in children and adults with SCD. Because of the risks associated with ACS and its unpredictable course, conservative management with admission for intervention or observation irrespective of disease severity is normative.[28,29] Risk factors for developing ACS include respiratory infections, treatment with opiates, and splinting due to chest or abdominal pain.[30]

Treatment of ACS includes empiric antimicrobial coverage with a third-generation cephalosporin and a macrolide to cover community-acquired and atypical pneumonia as well as encapsulated organisms. In treating pain and dehydration, the clinician balances the benefit of aggressive pain treatment and fluid resuscitation against the risks of respiratory depression with opiate administration and fluid overload. Hydration with fluids at a rate between two-thirds and maintenance is sufficient. In the absence of an additional indication for transfusion, such as severe anemia or worsening clinical status, transfusions are not emergently indicated.[31] A recent Cochrane Review concluded that insufficient evidence supports the empiric use of short-acting bronchodilators for SCD patients; however, given the incidence of comorbid asthma in children with SCD, a trial of therapy may be warranted.[32-34] Historically, corticosteroids were used to treat ACS, but this practice is discouraged because corticosteroids are associated with severe rebound vaso-occlusive crises, stroke, and death. If they must be used due to severity of respiratory distress, conservative tapering is indicated.[35]

Asthma. The prevalence of asthma in children with SCD is similar to the prevalence in children of African descent in the United States.[36] Children with SCD and asthma have higher SCD morbidity and increased rates of ACS, vaso-occlusive pain crisis (VOC), and premature mortality compared to those without asthma.[37] Wheezing is common in children with SCD and may portend intrinsic SCD-related pulmonary disease rather than reactive airway disease. Acute episodes of wheezing in the setting of ACS should be managed with inhaled beta-2 agonists and, if necessary, corticosteroids with careful tapering.[38] See Table 3 for specific management.

Musculoskeletal

Vaso-occlusive pain crisis. Acute VOC pain crisis is the hallmark of SCD. Patients present with severe pain as early as 6 months of age. Of note, most sickle cell-related pain in children is managed at home with supportive care and oral pain medications. Hydroxyurea is the only medicine that decreases the pain crisis frequency.[6,26,39,40] In older children and adolescents, VOC pain is often symmetric and regional, usually in the back or extremities, although it can affect any part of the body. Parents are often familiar with their child's pattern of pain. Verbal children may be able to describe the pain as typical or atypical for their painful crisis. Identification of children experiencing painful crises facilitates early triage, prompt pain medication administration, and evaluation for potential alternate etiologies of pain such as ACS, cholecystitis, osteomyelitis, constipation, and osteonecrosis.

Dactylitis, or hand-foot syndrome, is a painful complication of SCD affecting young children, typically 6 months to 2 years of age and rarely after 5 years of age. Ischemia and

Figure 1. Oxygenated peripheral blood smears from individuals with sickle cell anemia (A), hemoglobin SC disease (B), sickle β⁰-thalassemia (C), Homozygous hemoglobin C (D), and Hemoglobin SD disease (E)

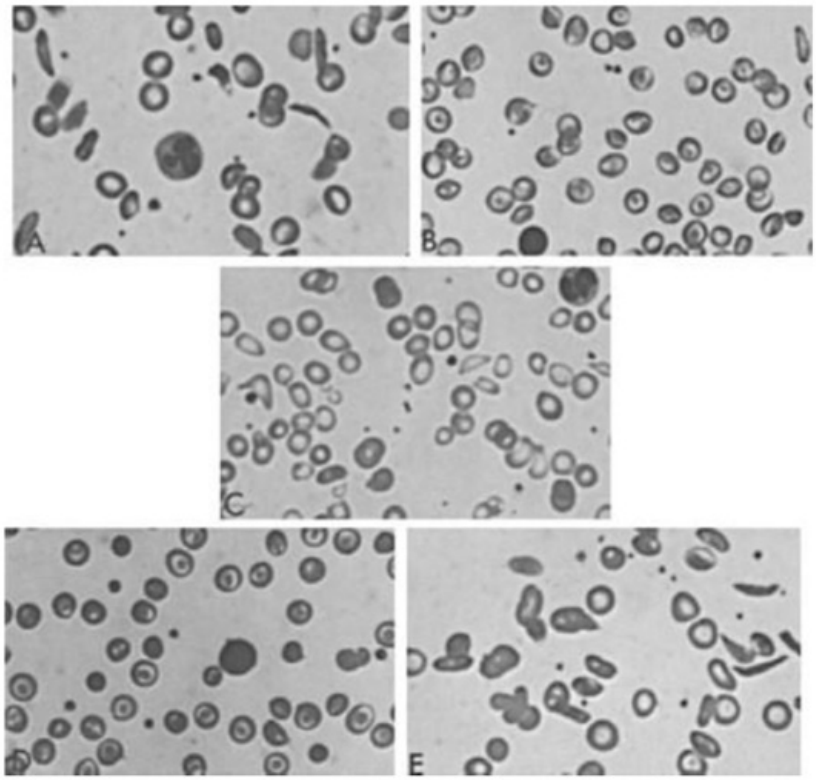
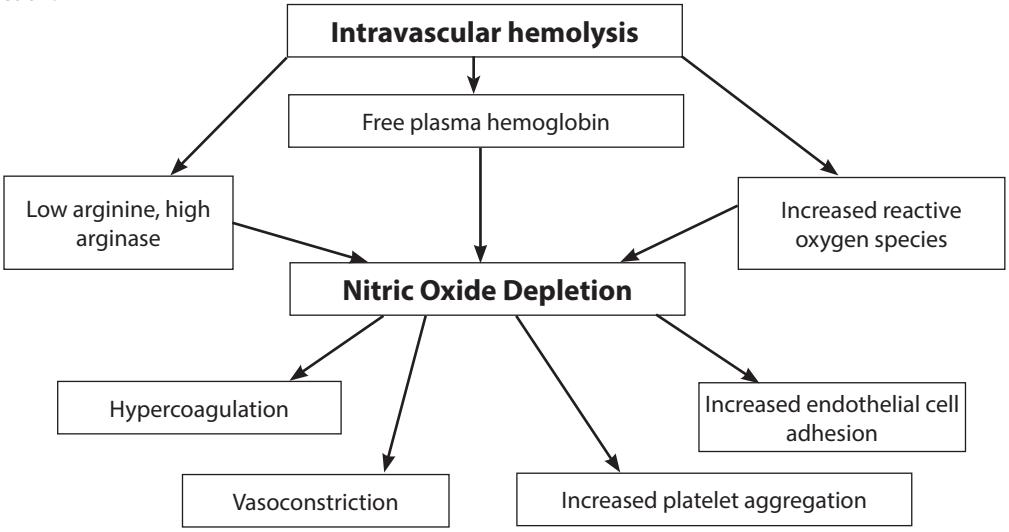


Figure 2. Intravascular Hemolysis

Intravascular hemolysis leads to nitric oxide depletion, resulting in hypercoagulation, vasoconstriction, and platelet aggregation and endothelial dysfunction.



Adapted from: Nathan and Oski's Hematology of Infancy and Childhood, Chapter 19, Seventh Edition.

Table 3. Management of Wheezing in Children with SCD

Acute Wheezing *and*	
a. ACS with h/o asthma	Bronchodilator and short course steroids
b. ACS with no prior h/o asthma	Careful history of atopy; high suspicion treat as above; low suspicion use bronchodilator and single-dose steroid
Acute Wheezing *and*	
a. No ACS with h/o asthma	Bronchodilator and short course steroids; start controller medications for those with persistent asthma
b. No ACS with no h/o asthma	Careful history of atopy, high suspicion follow a. If low suspicion, follow bronchodilator and single dose of steroid and discharge with bronchodilator

* Short course of corticosteroids include single dose dexamethasone 0.3-0.6 mg/kg (max 10 mg) or prednisone 2 mg/kg (max 60 mg X 3 days)
* Systemic steroids longer than 1-2 days are associated with rebound pain, fat necrosis, and intracranial hemorrhage.

Adapted from Glassberg et al. Wheezing in children with sickle cell disease. *Curr Opin Pediatr* 2014;26:9-18.

infarction of the metacarpals and phalanges cause painful and often symmetric swelling of hands and/or feet and sometimes fever. This may occur in isolation or during a VOC event, and, although dactylitis may cause fever, blood culture and parenteral antibiotics are indicated (see: Fever).

Evaluation

On physical exam, VOC pain is not usually accompanied by edema or erythema, although patients may be tender at the site of pain. Evaluating and treating sickle cell VOC is vexing to clinicians because of the dependence on subject pain reports. Pain scales may not accurately reflect patient pain, and over reliance on such scales may lead to under treatment of pain and seriously compromise patient care.[3] Vital signs and general appearance may be discordant with the patient's report of pain. In these instances, communication between parents, patients, and, whenever possible, the primary hematology team help optimize the pain management plan.

Management

Rapid triage, evaluation by a clinician, and early administration of opioid analgesia are the mainstay of treatment for an acute pain crisis.[21] Isotonic fluids should be administered only if patients appear dehydrated as they may exacerbate hemolysis; otherwise, half normal saline at maintenance rate is the mainstay. Clinical care pathways for VOC expedite management, decrease time to first analgesia, and improve patient satisfaction.[41] Laboratory evaluation should include CBC, reticulocyte count, liver function tests, and bilirubin levels. No laboratory values can confirm a painful crisis. CRP and LDH are often elevated, signifying the nonspecific presence of inflammation and hemolysis, respectively. Trials are underway to identify genes that are upregulated in acute painful crisis.

When possible, ED staff should have access to pain plans developed by the patient in consultation with his/her primary hematologist or primary provider. Individualized pain plans decrease hospitalization and readmission rates.[8] Mild pain can be managed with NSAIDs and hydration, but severe pain requires opiates. Morphine and hydromorphone are the drugs most widely used, and when renal function is adequate, ketorolac may be used as adjunct therapy.[21] If available and developmentally appropriate, a patient-controlled analgesia pump should be initiated promptly. Nonpharmacological measures, such as distraction, acupressure, relaxation, and music, can be helpful in early or mild pain but no randomized clinical trials compare their efficacy to medication.[9] Other agents under investigation for treatment of VOC in children include low-dose subcutaneous ketamine,[42,43] nitric oxide,[44] and magnesium.[1,5,45]

Avascular necrosis (AVN). AVN is a debilitating condition caused by osteonecrosis from compromised osseous circulation. Blood hyperviscosity[46] and RBC deformability[47] play an important roles in its pathogenesis. The femoral head is the most commonly affected site, causing severe and chronic hip pain. However, AVN may also occur in other joints such as the spine and shoulders. AVN is more commonly seen in HbSS in children < 15 years of age and those with a high hematocrit.[48] Treatment is usually conservative until surgical replacement is required.[4,6-8,21]

Infection

Fever and sepsis. Children with SCD are functionally asplenic and at increased risk of serious bacterial infections.[10-12,49] They are at particular risk for infection with encapsulated organisms (*Streptococcus pneumoniae*, *Haemophilus influenza*, and *Neisseria meningitidis*) and enteric Gram-negative organisms such as Salmonella. Penicillin prophylaxis and 23-valent pneumococcal vaccination have decreased the rate of bacteremia among children with SCD.[13-18,50] Nevertheless, any child with SCD and fever should be screened for bacterial infection with at least an aerobic blood culture. A complete history of a febrile child with SCD includes penicillin adherence for children younger than 5 years old, and attention to pneumococcus, *H. influenza*, and meningococcal vaccination status. Even in an optimally prophylaxed and vaccinated child, penicillin-resistant

organisms or non-vaccine pneumococcal serotypes may cause infection.[51]

The 2014 National Heart, Lung, and Blood Institute (NHLBI) guidelines define fever as a temperature > 38.5° C or 101.3° F. According to the new national standards, any child meeting this condition at home or in a health care setting needs: 1) immediate evaluation with a complete medical history and physical, CBC with reticulocyte count, blood culture and to consider a urine culture; and 2) prompt administration of a parenteral antibiotic that covers *S. pneumoniae* and Gram-negative organisms such as a third-generation cephalosporin. The NHLBI recommends admission of any ill-appearing children and those with risk factors for bacteremia, including infants younger than 6 months of age, CBC different from baseline, missed penicillin doses, pulmonary disease, or concern for ability to return for a second dose of antibiotics. Well-appearing children may be managed as outpatient if adequate resources for follow-up exist.

Given the increasingly diverse population of children with SCD in the United States, infections such as Ebola, malaria, or dengue must be considered if a child's travel history is consistent with potential exposure. Salmonella and *Staphylococcus aureus* cause osteomyelitis and should be considered in patients with fever and focal bony tenderness.[19-21]

Spleen

Splenic Sequestration. Splenic sequestration is an acute enlargement of the spleen with a fall in hemoglobin at least 20% from baseline. Reticulocyte count may be normal or increased,[53] and thrombocytopenia is common, as platelets are also sequestered in the spleen. Diagnosis of splenic sequestration is clinical. Imaging is not required. The median age in HbSS and HbSß^0 is 1-4 years, with episodes seen as early as 5 weeks.[21,54] In patients with HbSC and HbSß+, splenic involution is delayed and sequestration may present at an older age.[25,54] Parents are taught spleen palpation maneuvers because early identification and prompt treatment helps prevent severe presentations and death.[28,29,55]

Sickled red blood cells trapped in the splenic sinusoids cause mechanical obstruction leading to the clinical signs of sequestration: abdominal distension, pallor and hemodynamic instability with tachycardia, and hypotension. Alternative diagnoses in children with anemia and thrombocytopenia include transient aplastic crisis and chronic hypersplenism. Immediate resuscitation with intravenous fluids and emergent blood transfusion can be lifesaving. Transfusions should be administered in small aliquots. This is because the spleen releases RBCs and patients "auto-transfuse," releasing RBCs into the peripheral circulation and placing transfused patients at risk for hyperviscosity and stroke. Recurrence of splenic sequestration is common, recurring in 50-75% of cases. In some instances, splenectomy is indicated.[54,56]

Transient aplastic crisis. Human parvovirus B19 is now known to be the cause of transient aplastic crises in patients with SCD. Because SCD patients depend on their reticulocytes to maintain their hemoglobin, the reticulocyte suppression associated with parvovirus B19 can cause life-threatening anemia. Patients present with sudden onset of pallor, fatigue, and weakness and may have signs of high-output heart failure. Reticulocytopenia with anemia supports this diagnosis. Treatment is supportive, and RBC transfusion may be required. In severely anemic patients, RBC transfusion should be administered slowly, in small aliquots, as patients may have compensated for their severe anemia. Rapid transfusion may trigger high-output heart failure.[57] During the recovery phase, the CBC shows reticulocytosis with severe anemia, making splenic sequestration another possible differential concern.

If parvovirus infection is suspected in a patient in the ED, the patient should be isolated from common areas and strict droplet precautions applied. Pregnant or potentially pregnant staff should be assigned to other patients, as parvovirus may cause severe fetal complications.[58]

Gastrointestinal and Hepatobiliary

Gastrointestinal complications of SCD include cholelithiasis, abdominal VOC, and constipation. In young children especially, physical exam may be insufficient to distinguish these etiologies from causes of acute abdomen common in all children vs those particular to children with SCD. Here we discuss gastrointestinal complications of SCD, with the caution that these children may, like children without SCD, have acute abdominal pathology unrelated to SCD.[52]

Cholelithiasis/cholecystitis. Cholelithiasis occurs in 26-58% of patients with HbSS disease and is associated with higher baseline hyperbilirubinemia. Patients with cholelithiasis present with colicky abdominal pain that localizes to the upper right quadrant. The best first test for evaluation is ultrasound; however, the test is not sensitive for gallstones. Emergency management for pain associated with cholelithiasis is supportive with hydration and opiates. Because of chronic cholelithiasis, patients are at risk for cholecystitis. Primary management of this infectious complication of cholelithiasis includes parenteral antibiotics to cover anaerobic and gram-negative abdominal organisms; piperacillin-tazobactam is commonly used. For symptomatic cholelithiasis, cholecystectomy is often delayed until the patient is stable and asymptomatic, although this practice is debated.[52]

Neurologic

Stroke. Children with SCD are 333 times more likely to suffer a stroke than children in the general population.[59] Approximately 11% of children with SCD develop overt stroke before the age of 20 years. Children are at greatest risk from

2-5 years of age. Stroke is most common in HbSS and less in HbS-ß-thalassemia or HbSC disease.[59] Ischemic strokes constitute 54% of cerebrovascular accidents (CVA) in SCD patients and are more common in the very young and old. Hemorrhagic strokes are more common among patients with SCD in their 20s.[60] About 10-30% of children develop silent cerebral infarcts with T2 signal abnormalities in the white matter in the absence of overt neurological deficits.[61] Routine screening with transcranial Doppler allows early identification of children at risk for stroke and permits intervention with chronic RBC transfusion.[62] Children with a history of stroke may receive chronic blood transfusion to maintain HbS at less than 30%. This treatment reduces the risk of recurrent stroke from 70-90% to less than 20-30%.[63] Hydroxyurea and stem cell transplant are treatment options beyond the scope of this review.

Pathophysiology

Ischemic strokes initially were thought to result from hyperviscosity of sickled red cells with subsequent vasculopathy and stenosis of the large cerebral vessels branching off of the Circle of Willis.[60] It is now known that the mechanism is not that simple. It's an interplay of adhesion of sickled cells to the vascular endothelium and resultant ischemia-reperfusion injury that triggers release of prothrombotic factors resulting in microvascular occlusion and thrombosis.[24,60,64-66] Hemorrhagic stroke may result from rupture of the prevalent multiple small aneurysms, especially in the posterior circulation. Risk factors for CVA are described in Table 4.

Clinical Presentation

Children having a CVA may present with seizures and motor deficits, and posterior circulation lesions may present with ataxia. In some children, headache may be the only symptom. Hemorrhagic strokes present with severe headaches caused by meningeal irritation and increased intracranial pressure. In high-risk SCD patients, such as those with HbSS, a low threshold for brain imaging is warranted.[30,67]

Management

Stroke is a medical emergency and must be managed with an interdisciplinary team including the ED physician, radiologist, neurologist, and hematologist. The specialists responsible for exchange transfusion vary by center and may be transfusion medicine specialists or pathologists. These specialists should also be notified of any child with a likely stroke.

Initial assessment should focus on stabilization of the patient and monitoring vital signs. Where available, a stroke algorithm should be used. Initial management includes a detailed history and physical examination, CBC, reticulocyte count, type and screen, basic metabolic panel, and coagulation profile. A non-contrast CT scan determines hemorrhagic stroke and is often the first test available. MRI and MRA with diffusion-weighted images are the gold standard for identifying the timing and location of ischemic stroke and should be performed for all children with SCD in whom stroke is a differential concern.[63] Overnight MRI may be delayed due to availability of technicians or need for patient anesthesia. This need not delay manual or automated exchange transfusion. If technical or logistical challenges also obstruct exchange transfusion, simple transfusion may be used, but should not raise the hemoglobin to more than 10 g/dL due to the risk that hyperviscosity that may cause secondary stroke.[31,63] There is no role for antifibrinolytics or anticoagulation.

Table 4. Risk Factors for Stroke in SCD

Ischemic Stroke	Hemorrhagic Stroke	SCI
Prior ischemic stroke h/o TIA h/o SCI Nocturnal hypoxemia Recent ACS, fever or exchange transfusion within 2 weeks of stroke TCD velocity ≥ 200cm/sec	Hypertension Older age Low Hb	Baseline leukocytosis Baseline low Hb h/o seizures

Adapted from: Verduzco LA, Nathan DG. Sickle cell disease and stroke. *Blood* 2009;114:5117-5125.

Genitourinary

Priapism. Priapism (prolonged erection unrelated to sexual stimulus) is common in boys and men with SCD and is responsible for 65% of all cases of major priapism (lasting > 4 hours).[32-34,68] At least 35% of men with SCD experience priapism.[21,35] The mean age at first attack is 15 years, and 75% will have their first attack before 20 years of age.[36,69]

Priapism is a urologic emergency. Recurrent, untreated episodes cause long-term damage to penile structure and function.[37,70] Prolonged intervals of priapism (> 48 hours) are associated with increased risk of erectile dysfunction, regardless of intervention. Priapism is incompletely understood but likely attributable to penile venous stasis, hypoxia, and ischemia.[38,71]

It is important to ascertain the duration of symptoms, degree of pain, history of priapism, drug use (recreational or medicinal), and self-treatment attempts. Combined with careful physical exam, this may exclude alternate etiologies for priapism, even in patients with SCD.[37,70] Initial laboratory testing includes CBC, hemolysis markers, and type and screen.

No large randomized trials guide emergency management of sickle cell-related priapism. The emergent goal of treatment is detumescence.

Initial management is conservative with hydration, oxygen, and pain control with opiates. Oral alpha-adrenergic agents such as pseudoephedrine (0.5 mg/kg to a maximum dose of 30 mg) may be used, although no trial definitively demonstrates efficacy.[21] For major priapism (> 4 hours) or priapism unresponsive to conservative intervention, urology consultation should be obtained for potential corporeal aspiration and/or alpha-adrenergic intracorporeal injection.[41,68] Blood transfusions are associated with adverse neurologic events in the setting of priapism and should be avoided if possible.[21,70] The need for anesthesia to emergently treat priapism may require a blood transfusion and should prompt hematology consultation.

Surgery

Whenever possible, children with SCD requiring emergent surgery should be transfused in consultation with a hematologist prior to receiving anesthesia. In a trauma setting this may not be possible. The goal of transfusion is to reduce the fraction of sickle cells in circulation. Transfusion prior to low-risk surgery reduces the risk of postoperative complications, particularly for patients with HbSS.[72] As a rule of thumb, 5 mL/kg of packed RBCs raises the hemoglobin 1 g/dL. In patients with a hemoglobin level close to 10 g/dL, simple transfusion may not be possible due to the risk of hyperviscosity.

Conclusion

Clinicians in the ED play a critical role in identifying and treating the many complications of SCD. A careful patient history, physical exam, and review of laboratory testing should guide the ED clinician's evaluation and treatment of SCD patients. Children with SCD benefit from treatment algorithms for many common complications of their disease. Whenever possible, access to records and communication with treating hematologists is valuable.

References

1. Piel FB, Tatem AJ, Huang, et al. Global migration and the changing distribution of sickle haemoglobin: A quantitative study of temporal trends between 1960 and 2000. *Lancet Glob Health* 2014;2:e80-e89.
2. Aygun B, Mortier NA, Smeltzer MP, et al. Hydroxyurea treatment decreases glomerular hyperfiltration in children with sickle cell anemia. *Am J Hematol* 2013;88:116-119.
3. Ballas SK. Ethical issues in the management of sickle cell pain. *Am J Hematol* 2001;68:127-132.
4. Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Improved survival of children and adolescents with sickle cell disease. *Blood* 2010;115:3447-3452.
5. Piel FB, Hay SI, Gupta S, et al. Global burden of sickle cell anaemia in children under five, 2010–2050: Modelling based on demographics, excess mortality, and interventions. *PLoS Med* 2013;10:e1001484. doi: 10.1371/journal.pmed.1001484. Epub 2013 Jul 16.
6. Thornburg CD, Files BA, Luo Z, et al. Impact of hydroxyurea on clinical events in the BABY HUG trial. *Blood* 2012;120:4304-4310.
7. Angelucci E, Matthes-Martin S, Baronciani D, et al. Hematopoietic stem cell transplantation in thalassemia major and sickle cell disease: Indications and management recommendations from an international expert panel. *Haematologica* 2014;99:811-820.
8. Hsieh MM, Fitzhugh CD, Weitzel RP, et al. Nonmyeloablative HLA-matched sibling allogeneic hematopoietic stem cell transplantation for severe sickle cell phenotype. *JAMA* 2014;312:48-56.
9. Ballas SK. Current issues in sickle cell pain and its management. *Hematology Am Soc Hematol Educ Program* 2007; 97-105.
10. Darbari DS, Kple-Faget P, Kwagyan J, et al. Circumstances of death in adult sickle cell disease patients. *Am J Hematol* 2006;81:858-863.
11. Platt OS, Brambilla DJ, Rosse WF, et al. Mortality in sickle cell disease — Life expectancy and risk factors for early death. *N Engl J Med* 1994;330: 1639-1644.
12. Powars DR, Chan LS, Hiti A, et al. Outcome of sickle cell anemia: A 4-decade observational study of 1056 patients. *Medicine (Baltimore)* 2005;84:363-376.
13. Lovett PB, Sule HP, Lopez BL. Sickle cell disease in the emergency department. *Emerg Med Clin North Am* 2014;32:629-647.
14. Glassberg JA, Wang J, Cohen R, et al. Risk factors for increased ED utilization in a multinational cohort of children with sickle cell disease. *Acad Emerg Med* 2012;19:664-672.
15. Panepinto JA, Owens PL, Mosso AL, et al. Concentration of hospital care for acute sickle cell disease-related visits. *Pediatr Blood Cancer* 2012;59:685-689.
16. Bundy DG, Strouse JJ, Casella JF, Miller MR. Urgency of emergency department visits by children with sickle cell disease: A comparison of 3 chronic conditions. *Acad Pediatr* 2011;11:333-341.
17. Stein DM, Flum AS, Cashy J, et al. Nationwide emergency department visits for priapism in the United States. *J Sex Med* 2013;10:2418-2422.
18. Roghmann F, Becker A, Sammon JD, et al. Incidence of priapism in emergency departments in the United States. *J Urol* 2013;190:1275-1280.
19. Jan S, Slap G, Smith-Whitley K, et al. Association of hospital and provider types on sickle cell disease outcomes. *Pediatrics* 2013;132:854-861.
20. Glassberg JA, Tanabe P, Chow A, et al. Emergency provider analgesic practices and attitudes toward patients with sickle cell disease. *Ann Emerg Med* 2013;62:293-302.e10.
21. National Heart, Lung, and Blood Institute. Evidence-based Management of Sickle Cell Disease. Available at: http://www.nhlbi.nih.gov/sites/www.nhlbi.nih.gov/files/sickle-cell-disease-report.pdf. Accessed Jan. 6, 2015.
22. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: Summary of the 2014 evidence-based report by expert panel members. *JAMA* 2014;312:1033-1048.
23. Brandow AM, Liem RI. Sickle cell disease in the emergency department: Atypical complications and management. *Clin Pediatr Emerg Med* 2011;12:202-212.
24. Hebbel RP, Osarogiagbon R, Kaul D. The endothelial biology of sickle cell disease: Inflammation and a chronic vasculopathy. *Microcirculation* 2004;11:129-151.
25. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. *Lancet* 2010;376:2018-2031.
26. Ware RE. How I use hydroxyurea to treat young patients with sickle cell anemia. *Blood* 2010;115:5300-5311.
27. Miller ST, Rey K, He J, et al. Massive accidental overdose of hydroxyurea in a young child with sickle cell anemia. *Pediatr Blood Cancer* 2012;59:170-172.
28. Mekontso Dessap A, Deux JF, Habibi A, et al. Lung imaging during acute

chest syndrome in sickle cell disease: Computed tomography patterns and diagnostic accuracy of bedside chest radiograph. *Thorax* 2014;69:144-151.
29. Creary SE, Krishnamurti L. Prodromal illness before acute chest syndrome in pediatric patients with sickle cell disease. *J Pediatr Hematol Oncol* 2014;36: 480-483.
30. Srinivasan A, Wang WC, Gaur A, et al. Prospective evaluation for respiratory pathogens in children with sickle cell disease and acute respiratory illness. *Pediatr Blood Cancer* 2013;61:507-511.
31. Saylors RL, Watkins B, Saccente S, Tang X. Comparison of automated red cell exchange transfusion and simple transfusion for the treatment of children with sickle cell disease acute chest syndrome. *Pediatr Blood Cancer* 2013;60:1952-1952. doi:10.1002/pbc.24744.
32. Knight-Madden JM, Hambleton IR. Inhaled bronchodilators for acute chest syndrome in people with sickle cell disease. *Cochrane Database Syst Rev* 2014;8:CD003733.
33. DeBaun MR, Rodeghier M, Cohen R, et al. Factors predicting future ACS episodes in children with sickle cell anemia. *Am J Hematol* 2014;89:E212-217. doi:10.1002/ajh.23819.
34. Williams SN, Nussbaum E, Yoonessi L, et al. Progression and prognostic indicators of bronchial disease in children with sickle cell disease. *Lung* 2014;192: 385-393.
35. Ogunlesi F, Heeney MM, Koumbourlis AC. Systemic corticosteroids in acute chest syndrome: Friend or foe? *Paediatr Respir Rev* 2014;15:24-27.
36. Boyd JH, Moinuddin A, Strunk RC, DeBaun MR. Asthma and acute chest in sickle-cell disease. *Pediatr Pulmonol* 2004;38:229-232.
37. Glassberg JA, Strunk R, DeBaun MR. Wheezing in children with sickle cell disease. *Curr Opin Pediatr* 2014;26:9-18.
38. Darbari DS, Catro O, Taylor JG 6th, et al. Severe vaso-occlusive episodes associated with use of systemic corticosteroids in patients with sickle cell disease. *J Natl Med Assoc* 2008;100:948-951.
39. Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle-cell anaemia: A multicentre, randomised, controlled trial (BABY HUG). *Lancet* 2011;377: 1663-1672.
40. Charache S, Terrin ML, Moore RD, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. *N Engl J Med* 1995;332: 1317-1322.
41. Ender KL, Krajewski JA, Babineau J, et al. Use of a clinical pathway to improve the acute management of vaso-occlusive crisis pain in pediatric sickle cell disease. *Pediatr Blood Cancer* 2014;61:693-696.
42. Neri CM, Pestieau SR, Darbari DS. Low-dose ketamine as a potential adjuvant therapy for painful vaso-occlusive crises in sickle cell disease. *Paediatr Anaesth* 2013;23:684-689.
43. Uprety D, Baber A, Foy M. Ketamine infusion for sickle cell pain crisis refractory to opioids: A case report and review of literature. *Ann Hematol* 2014;93:769-771. doi:10.1007/s00277-013-1954-3.
44. Gladwin MT, Kato GJ, Weiner D, et al. Nitric oxide for inhalation in the acute treatment of sickle cell pain crisis: A randomized controlled trial. *JAMA* 2011;305:893-902.
45. Badaki-Makun O, Scott JP, Panepinto JA, et al. Intravenous magnesium for pediatric sickle cell vaso-occlusive crisis: Methodological issues of a randomized controlled trial. *Pediatr Blood Cancer* 2014;61:1049-1054.
46. Kato GJ, Gladwin M, Steinberg M. Deconstructing sickle cell disease: Reappraisal of the role of hemolysis in the development of clinical subphenotypes. *Blood Rev* 2007;21:37-47.
47. Lemonne N, Lamarre Y, Romana M, et al. Does increased red blood cell deformability raise the risk for osteonecrosis in sickle cell anemia? *Blood* 2013;121:3054-3056.
48. Milner PF, Kraus AP, Sebes JI, et al. Sickle cell disease as a cause of osteonecrosis of the femoral head. *N Engl J Med* 1991;325:1476-1481.
49. Booth C, Inusa B, Obaro SK. Infection in sickle cell disease: a review. *Int J Infect Dis* 2010;14:e2-e12.
50. Baskin MN, Goh XL, Heeney MM, Harper MB. Bacteremia risk and outpatient management of febrile patients with sickle cell disease. *Pediatrics* 2013;131:1035-1041.
51. McCavit TL, Quinn CT, Techasaensiri C, Rogers ZR. Increase in invasive Streptococcus pneumoniae infections in children with sickle cell disease since pneumococcal conjugate vaccine licensure. *J Pediatr* 2011;158:505-507.
52. Ebert EC, Nagar M, Hagspiel KD. Gastrointestinal and hepatic complications of sickle cell disease. *Clin Gastroenterol Hepatol* 2010;8:483-489.
53. Topley JM, Rogers DW, Stevens MC, Serjeant GR. Acute splenic sequestration and hypersplenism in the first five years in homozygous sickle cell disease. *Arch Dis Child* 1981;56:765-769.
54. Brousse V, Elie C, Benkerrou M, et al. Acute splenic sequestration crisis in sickle cell disease: cohort study of 190 paediatric patients. *Br J Haematol* 2012;156:643-648.
55. Brousse V, Buffet P, Rees D. The spleen and sickle cell disease: The sick(led) spleen. *Br J Haematol* 2014;166:165-176.
56. Allareddy V, Roy A, Lee MK, et al. Outcomes of acute chest syndrome in adult patients with sickle cell disease: Predictors of mortality. *PLoS ONE* 2014;9:e94387.
57. Quinn CT. Sickle cell disease in childhood: From newborn screening through transition to adult medical care. *Pediatr Clin North Am* 2013;60:1363-1381.
58. Dijkmans AC, de Jong EP, Dijkmans BA, et al. Parvovirus B19 in pregnancy: Prenatal diagnosis and management of fetal complications. *Curr Opin Obstet Gynecol* 2012;24:95-101.
59. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cerebrovascular accidents in sickle cell disease: Rates and risk factors. *Blood* 1998;91:288-294.
60. Verduzco LA, Nathan DG. Sickle cell disease and stroke. *Blood* 2009;114: 5117-5125.
61. DeBaun MR, Gordon M, McKinstry RC, et al. Controlled trial of transfusions for silent cerebral infarcts in sickle cell anemia. *N Engl J Med* 2014;371:699-710.
62. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med* 1998;339:5-11.
63. Webb J, Kwiatkowski JL. Stroke in patients with sickle cell disease. *Expert Rev Hematol* 2013;6:301-316.
64. Kaul DK, Fabry ME, Costantini F, et al. In vivo demonstration of red cell-endothelial interaction, sickling and altered microvascular response to oxygen in the sickle transgenic mouse. *J Clin Invest* 1995;96:2845-2853.
65. Kaul DK, Fabry ME, Nagel RL. The pathophysiology of vascular obstruction in the sickle syndromes. *Blood Rev* 1996;10:29-44.
66. Hatzipantelis ES, Pana ZD, Gombakis N, et al. Endothelial activation and inflammation biomarkers in children and adolescents with sickle cell disease. *Int J Hematol* 2013;98:158-163.
67. Armstrong FD, Thompson RJ Jr, Wang W, et al. Cognitive functioning and brain magnetic resonance imaging in children with sickle cell disease.

Neuropsychology Committee of the Cooperative Study of Sickle Cell Disease. *Pediatrics* 1996;97:864-870.
68. Donaldson JF, Rees RW, Steinbrecher HA. Priapism in children: A comprehensive review and clinical guideline. *J Pediatr Urol* 2014;10:11-24.
69. Anele UA, Kyle Mack A, Resar LM, Burnett AL. Hydroxyurea therapy for priapism prevention and erectile function recovery in sickle cell disease: A case report and review of the literature. *Int Urol Nephrol* 2014;46:1733-1736.
70. Olujohungbe A, Burnett AL. How I manage priapism due to sickle cell disease. *Br J Haematol* 2013;160:754-765.
71. Bivalacqua TJ, Musicki B, Kutlu O, Burnett AL. New insights into the pathophysiology of sickle cell disease-associated priapism. *J Sex Med* 2012;9:79-87.
72. Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease. Cooperative Study of Sickle Cell Diseases. *Blood* 1995;86:3676-3684.

CME Questions

1. A 3-year-old boy with known sickle cell disease (HbSS) presents to the emergency department with his mother after she saw his right arm jerking rhythmically for several minutes. The movement stopped spontaneously and the child is talkative in the exam room. On neurological exam, you think he has 4/5 strength on his right hand grasp. Which of the following is recommended?
   a. Head CT
   b. Consult neurology
   c. Complete blood count, reticulocyte count, and type and screen
   d. Consult hematology
   e. All of the above
2. A 15-year-old girl with sickle cell disease (HbSßo) presents with 3 days of worsening pain in her chest, arms, and legs. She describes the pain as typical of her painful crises. She has been treated at home with ibuprofen and oxycodone. Her mother denies fever. On physical exam, her vital signs are Temp 99.0°, BP 100/60, HR 100, RR 20, SaO_2 99%, and her exam is normal except for reproducible tenderness at her pain sites. A nurse administers the dose of morphine you ordered. What are the additional management steps for this patient?
   a. This is a painful crises, no further evaluation is required
   b. Complete blood count, reticulocyte count, complete metabolic panel
   c. Complete blood count, reticulocyte count, complete metabolic panel and chest X-ray
   d. Complete blood count, reticulocyte count, complete metabolic panel, chest X-ray and administer oxygen
   e. Complete blood count, reticulocyte count, complete metabolic panel, blood culture, Chest X-ray, administer oxygen and ceftriaxone
3. A 7-year-old boy with sickle cell disease (HbSS) presents to the emergency department with fever and fatigue. His mother reports that he is usually very active, but has been content lying on the couch for the last few days. A stat CBC shows a hemoglobin of 5.5 g/dL and a reticulocyte count of 0.9%. What is the next step?
   a. Order droplet precautions and notify any potentially pregnant caregivers
   b. Order a 15 cc/kg red blood cell transfusion
   c. Order ceftriaxone and azithromycin
   d. Order a NS bolus 20cc/kg
4. A 4-year-old girl with sickle cell disease (HbSC) presents to the emergency department with a fever of 103.2° F at home. Her mother reports that she has been tugging on her right ear and fussier than usual. On physical exam, her HR is 110, RR is 27, BP is 95/50, and temperature is 101.7°. She squirms and cries during otoscopic exam, which reveals a right tympanic membrane that is red and bulging. The remainder of her exam is normal. The

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

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4. After completing the test, your browser will be directed to the activity evaluation form.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

best management for this patient includes which of the following?
   a. Amoxicillin 90 mg/kg divided BID for 10 days
   b. Ceftriaxone every 24 hours for at least two doses
   c. CBC, blood culture and Amoxicillin 90 mg/kg divided BID for 10 days
   d. CBC, blood culture and ceftriaxone every 24 hours for at least two doses

5. A 16-year-old girl with sickle cell disease (HbSS) disease taking hydroxyurea presents to the emergency department with fever to 101.6° F at home, cough, and runny nose. Her brother, a preschooler, has had similar symptoms. On physical exam, she has rhinorrhea and her lungs are clear to auscultation. You order blood culture, complete blood count, and a chest X-ray. You are surprised when her CBC shows: Hb 7.5 gm/dL, MCV 107 fL, WBC 3.7 k/mcL, absolute neutrophil count of .65k/mcL, and platelets 98 k/mcl. While the lab reviews the peripheral smear, you surmise that the most likely cause of these findings is:
   a. a new presentation of leukemia.
   b. this is a normal CBC for an adolescent with sickle cell disease.
   c. hydroxyurea toxicity.
   d. viral suppression.

6. Which of the following complications of sickle cell disease is an absolute indication for blood transfusion?
   a. Vaso-occlusive crises
   b. Acute chest syndrome
   c. Dactylitis
   d. Stroke
   e. Splenic sequestration

7. This is the third visit in month for a 12-year-old boy for right hip pain. Each time he was treated with intravenous morphine and his pain got better and he was discharged home. This time, his pain does not respond to the narcotics and he starts limping. What is your next step?
   a. Admit him for pain management
   b. Discharge him from the emergency room for drug-seeking behavior
   c. Reassess his history and physical for possible avascular necrosis of hip
   d. Get MRI to rule out osteomyelitis

8. An 8-year-old boy with HbS-ß+ thalassemia presents with wheezing for 3 days, runny nose, and cough. On exam, he is afebrile, RR 30, O_2 sats 97% on room air, and has bilateral expiratory wheezing. He has no prior h/o wheezing. What is your best next step?
   a. Get CXR, start antibiotics for acute chest syndrome
   b. Get CXR and give inhaled beta-2 agonists and short course of steroids
   c. Get CXR, detailed history of atopy and give inhaled beta-2 agonists and short course of steroids
   d. Since he has no prior history of wheezing and CXR is negative treat as mild upper respiratory illness.

PEDIATRIC EMERGENCY MEDICINE REPORTS

CME Objectives

Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in pediatric patients presenting to the emergency department;
- describe the epidemiology, etiology, pathophysiology, historical and examination findings associated with conditions in pediatric patients presenting to the emergency department;
- formulate a differential diagnosis and perform necessary diagnostic tests;
- apply up-to-date therapeutic techniques to address conditions discussed in the publication;
- discuss any discharge or follow-up instructions with patients.

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PEDIATRIC EMERGENCY MEDICINE **REPORTS**

Practical, Evidence-Based Reviews in Pediatric Emergency Care

Sickle Cell Emergencies

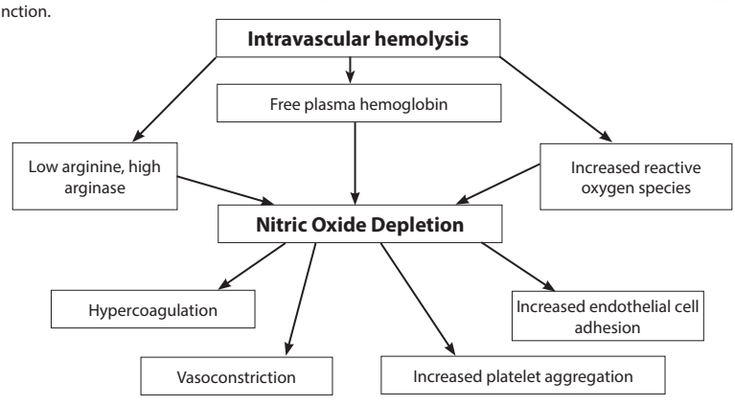
Classification of Sickle Cell Disease

Genotype	Hemoglobin Quantification in %					Phenotype (severity of disease and baseline range of Hb)
	HbA	HbS	HbF	HbC	HbA2	
HbAA (normal)	96	-	2	-	2	Normal
HbAS (trait)	50	45	2	-	2	Normal
HbSS	-	96	2	-	2	Severe, Hb 6-9 g/dL
HbSC	-	48	3	47	2	Moderate severe; stroke much less common. Hb 9-12 g/dL
HbSß$^+$	6	85	5	-	4	Moderate severe, Hb 10-13 g/dL
HbSß^0	-	93	2	-	5	Severe, Hb 6-9 g/dL

Adapted from: Glassberg J. Evidence-based management of sickle cell disease in the emergency department. *Emerg Med Pract* 2011;13:3 and Quinn C T. Sickle cell disease in childhood: From newborn screening through transition to adult medical care. *Pediatr Clin North Am* 2013;60:1363-1381.)

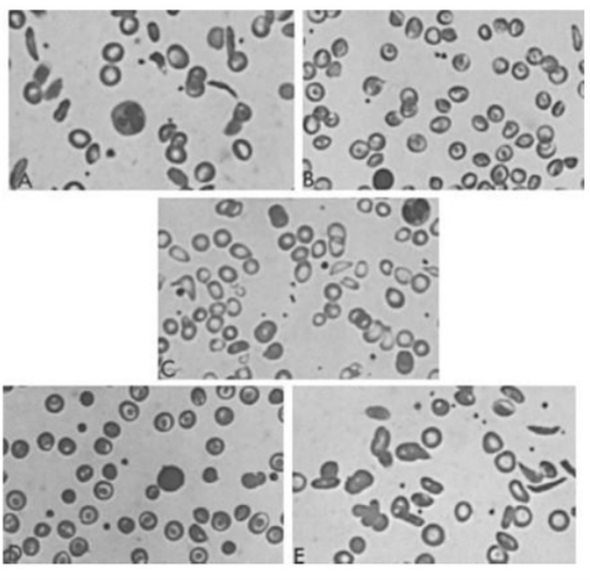
Intravascular Hemolysis

Intravascular hemolysis leads to nitric oxide depletion, resulting in hypercoagulation, vasoconstriction, and platelet aggregation and endothelial dysfunction.



Adapted from: Nathan and Oski's Hematology of Infancy and Childhood, Chapter 19, Seventh Edition.

Oxygenated peripheral blood smears from individuals with sickle cell anemia (A), hemoglobin SC disease (B), sickle β^0-thalassemia (C), Homozygous hemoglobin C (D), and Hemoglobin SD disease (E)



Common Studies in Patients with Sickle Cell Disease

Test	Significance
CBC	Anemia is expected; baseline varies and is influenced by genotype and clinical condition; leukocytosis and thrombocytosis are common during inflammatory crises — VOC, ACS, osteomyelitis; thrombocytopenia may indicate hepatic or splenic sequestration. Hydroxyurea may cause pancytopenia.
Reticuloctye Count	Given short t1/2 of sickle cell erythrocytes, patients are dependent on robust reticulocyte production to maintain their hemoglobin. A low reticulocyte count may be found as a harbinger of aplastic crisis or during such crises. Hydroxyurea also suppresses the reticulocyte count.
Liver Function Tests	Indirect hyperbilirubinemia is common. When possible, compare obtained value with historic values. If elevated above baseline, consider hemolytic crisis or cholelithiasis especially if accompanied by direct hyperbilirubinemia. AST is usually modestly elevated due to hemolysis. Hydroxyurea toxicity may cause elevations in AST and ALT.
Hemoglobin Quantitation	Values are reported as a percent and represent the types of hemoglobin present. Interpretation guides genotype diagnosis. The goal of emergent exchange transfusion is to decrease the HbS to at least 30% (equal to the HbS fraction in patients with HbAS.
Blood culture	Aerobic blood cultures should be drawn on any sickle cell patient with fever or in whom a bacterial infection is otherwise suspected.
Chest XR	Indicated for any patient with chest pain, fever or cough. Findings of a new infiltrate makes the diagnosis of acute chest syndrome
Head CT	If MRI is not immediately available or practical, non-contrast head CT should be used as a first line test in patients with headache, seizure or focal weakness in whom stroke is a concern. If negative and ongoing concern, MRI should be obtained.
Diffusion Weighted MRI	The most sensitive and specific study to define cerebrovascular accidents in children with sickle cell disease. Practical considerations may limit their emergent use — young patients may require sedation and technical expertise may be limited after hours.

Management of Wheezing in Children with SCD

Acute Wheezing *and*	
a. ACS with h/o asthma	Bronchodilator and short course steroids
b. ACS with no prior h/o asthma	Careful history of atopy; high suspicion treat as above; low suspicion use bronchodilator and single-dose steroid
Acute Wheezing *and*	
a. No ACS with h/o asthma	Bronchodilator and short course steroids; start controller medications for those with persistent asthma
b. No ACS with no h/o asthma	Careful history of atopy, high suspicion follow a. If low suspicion, follow bronchodilator and single dose of steroid and discharge with bronchodilator

* Short course of corticosteroids include single dose dexamethasone 0.3-0.6 mg/kg (max 10 mg) or prednisone 2 mg/kg (max 60 mg X 3 days)
* Systemic steroids longer than 1-2 days are associated with rebound pain, fat necrosis, and intracranial hemorrhage.

Adapted from Glassberg et al. Wheezing in children with sickle cell disease. *Curr Opin Pediatr* 2014;26:9-18.

Risk Factors for Stroke in SCD

Ischemic Stroke	Hemorrhagic Stroke	SCI
Prior ischemic stroke h/o TIA h/o SCI Nocturnal hypoxemia Recent ACS, fever or exchange transfusion within 2 weeks of stroke TCD velocity ≥ 200cm/sec	Hypertension Older age Low Hb	Baseline leukocytosis Baseline low Hb h/o seizures

Adapted from: Verduzco LA, Nathan DG. Sickle cell disease and stroke. *Blood* 2009;114:5117-5125.

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