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Dr. Farel (CME question reviewer) owns stock in Johnson & Johnson. Dr. Kavanagh (peer reviewer) reports travel for Council for Change, an organization for improving sickle cell care supported by Pfizer. Dr. Schneider (editor), Dr. Stapczynski (editor), Ms. Light (nurse planner), Dr. Peterfy (author), Dr. Tomecsek (author), Ms. Mark (executive editor), Ms. Coplin (executive editor), and Ms. Hatcher (editorial group manager) report no financial relationships with companies related to the field of study covered by this CME activity.

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# Sickle Cell Emergencies

Sickle cell disease affects millions of people. Its complications and clinical manifestations are seen frequently in patients presenting to the emergency department (ED). Sickle cell disease affects virtually every organ system and predisposes patients to a variety of problems, many of which can be life-threatening. Because many of these issues can be misdiagnosed easily, it is essential for the emergency medicine provider to be familiar with their presentation, workup, diagnosis, and treatment.

This article provides an overview of the most frequently encountered complications associated with sickle cell disease seen in the ED. It will discuss recent guidelines and novel approaches to the treatment of entities such as acute chest syndrome, vaso-occlusive crisis, and stroke, as well as new treatments on the horizon. With this knowledge, the provider should gain an improved understanding regarding the recognition and management of sickle cell disease complications.

## Introduction

Sickle cell disease is one of the most common hereditary red blood cell disorders seen by U.S. ED providers. It is an autosomal recessive disease known to affect about 70,000 Americans and carried an economic burden of $475 million from 1989 to 1993.[1,2] Although it mostly affects African Americans, the disease can be seen in people of Mediterranean, Indian, and Middle Eastern descent. With 1.2 million new cases diagnosed worldwide each year, it is imperative that the ED provider be familiar with its presentation, diagnosis, and complications.[3]

If they are diagnosed early, treated effectively, and receive thorough education regarding complications, U.S. patients with sickle cell disease have life expectancies to 50 years of age or older.[4] Unfortunately, innovations regarding its management are infrequent because of the lack of funding and research for sickle cell disease.

While pain is the most frequent complaint the provider will encounter in the ED, the complications of sickle cell disease can be life-threatening and need to be recognized and treated early to reduce significant morbidity and mortality. (*See Table 1.*)

## Pathophysiology

In a normal, healthy adult, red blood cells contain three forms of hemoglobin: HbA, HbA2, and HbF. Each specific type of hemoglobin is made up of four total polypeptide chains, which are present in pairs. For example, HbA is made up of two α-globin and two β-globin chains, while HbA2 consists of two α-globin and two δ-globin chains. HbF, or fetal hemoglobin, is made of two α-globin and two γ-globin chains.

## EXECUTIVE SUMMARY

- Patients with sickle cell disease often present in acute pain due to vaso-occlusion. Opioids should be given early. Other causes of their pain should be considered.
- While most of the patients seen in the ED are high utilizers, it is important to remember that this population represents only about 20% of all patients with sickle cell disease. High utilizers should be treated and referred to a physician who specializes in sickle cell disease. The Sickle Cell Disease Association of America can help connect patients with providers.
- Acute chest syndrome should be considered in patients with new chest pain, shortness of breath, or hypoxia. Chest X-ray findings lag behind symptoms.
- Although sickle cell disease is a devastating disease, new treatments for vaso-occlusive crisis and new cures using CRISPR may be on the horizon.

Sickle cell disease occurs when there is a mutation in the β-globin on chromosome 11.[5] This mutation causes a substitution of adenine for thymine, which in turn replaces glutamic acid for valine at the sixth amino acid position. In a deoxygenated environment, valine interlocks on an adjacent chain and forms bundles of parallel rods called tactoids.[6] This bridge causes HbS polymerization, leading to the sickle appearance. (*See Figure 1.*) The once normal cell, now sickled and distorted, undergoes early destruction. This sickling initially is reversible when HbS is reoxygenated, but with repeated episodes of sickling, the cell membrane becomes damaged and the distortion becomes permanent.

Not only is the life span of the red blood cell significantly decreased, the unnatural shape also causes hyperviscosity and obstruction in the microvasculature.[5] This leads to hemolysis, intermittent vascular occlusion, and tissue ischemia. In the setting of vaso-occlusion, hypoxia worsens, acidosis increases, and further sickling occurs.[5] This repetitive cycle leads patients to seek care in the ED.

Sickle cell disease encompasses those individuals who are homozygous for the sickle cell gene, denoted by HbSS, as well as heterozygous for the sickle cell gene and hemoglobins other than normal adult hemoglobin, such as HbSC or HbSβ+ thalassemia. Patients with sickle cell trait have both the sickle cell gene and a normal adult hemoglobin (HbAS) and usually are asymptomatic. Under severe physiologic stress, such as high altitude or extreme physical exertion, sickle cell trait patients may experience splenic infarction, although this is uncommon, and there have been case reports of acute chest syndrome as well.

Common manifestations of sickle cell disease include splenic infarcts, complications in pregnancy, retinopathy, hematuria, renal medullary carcinoma, and renal papillary necrosis.[6] Routine treatment of these patients usually consists of hydration, pain control, and education. If the provider is not careful, subtleties may go unnoticed, and complications that may cause the patient significant harm can develop.

## Clinical Features

Because sickle cell disease can affect numerous parts of the body, patients may present to the ED with a variety of complaints including bone pain, chest pain, shortness of breath, abdominal pain, fever, generalized weakness, and fatigue. Hence, it is critical for the provider to be able to differentiate between other entities, such as pneumonia, septic arthritis, acute coronary syndrome, or appendicitis, that possibly could mimic sickle cell complications. The clinical presentation, diagnosis, and treatment of sickle cell disease is variable and is dependent on the body system affected. Admission requirements vary as well. For example, if pain is not well controlled, a patient likely will need to be admitted for additional doses of analgesia. Other indications for admission include acute chest syndrome, sepsis, white blood cell count (WBC) > 30,000 $mm^3$, hemoglobin < 5 g/dL or a precipitous drop below baseline, and thrombocytopenia.[7]

## Vaso-occlusive Pain Crisis

The most common reason for a patient with sickle cell disease to visit the ED is pain due to vaso-occlusive crisis.[6] This process usually is initiated by some external stressor, with cold temperatures, infection, dehydration, and high altitude being the most common. When a patient's red blood cells undergo sickling, hyperviscosity and sludging of the intravascular volume ensues, leading to obstruction and ultimately tissue infarction.[6] Over time, chronic pain and end organ damage occur with recurrent vaso-occlusive crises. Pain usually occurs in the bones of the extremities, back, and chest. Although experts have varying opinions on the use of pain scales in the ED, commonly used options include the 0-10 numerical rating scale and the Wong-Baker FACES Pain Rating Scale in children. The diagnosis is clinical and will not be evident on physical exam (for example, no fever, tachycardia, or hypertension). Historically, ED practitioners have relied on vital signs as an indicator for pain severity. In a retrospective study published in 2000, of 459 patients presenting with symptoms of vaso-occlusive crisis, none were found to be hypertensive.[8] Therefore, the provider should not rely on vital sign abnormalities as an indicator of pain. If fever, redness, warmth, or swelling is noted, the provider should seek an alternative diagnosis, such as sepsis, cellulitis, or septic arthritis.

Once patients present to the ED, it usually indicates that their home analgesia regimen has become insufficient to control the pain. Sickle cell disease patients usually are well informed regarding their pain tolerance and will not come to the hospital unless absolutely necessary. But some of these patients have multiple visits to the ED (35% of the sickle cell population are recurrent ED users[9]); therefore, providers may limit orders for pain control and assume the patients may

## Table 1. Complications of Sickle Cell Anemia

| | |
|---|---|
| Neurologic | Ischemic or hemorrhagic stroke<br>Cerebral aneurysm<br>Chronic pain syndrome<br>Neuropathic pain syndrome |
| Eye | Retinopathy |
| Pulmonary | Acute chest syndrome<br>Pulmonary hypertension |
| Cardiac | Cardiomegaly |
| Abdominal, GI | Mesenteric ischemia<br>Hepatic infarction<br>Cholelithiasis<br>Intrahepatic cholestasis<br>Splenic sequestration |
| Renal, GU | Hematuria<br>Renal infarction<br>Papillary necrosis<br>Renal failure<br>Priapism |
| Musculoskeletal | Acute vaso-occlusive pain crisis; bone, joint, and muscle pain<br>Osteomyelitis<br>Avascular necrosis of femoral head |
| Dermatologic | Leg ulcers |
| Infection | Osteomyelitis<br>Pneumonia<br>Urinary tract infection |
| Hematologic | Chronic hemolysis<br>Acute hemolytic crisis<br>Aplastic crisis<br>Hypercoagulability: pulmonary embolism and venous thrombosis |

Source: Reprinted with permission from: Tintinalli JE, Stapczynski JS, Ma OJ, et al. *Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York; McGraw Hill; 2016:1506.

be narcotic seeking. It has been well documented that these patients are significantly undertreated. Providers may believe patients are not experiencing real pain based on their calm demeanor and normal vital signs. Some patients may exaggerate their pain because of past experience with under-treatment. Inadequate pain control has been associated with more frequent visits to U.S. EDs[10] and other complications, including acute chest syndrome. When evaluating patients in the ED with suspected vaso-occlusive crisis, it is important to determine the severity of their pain and build trust to treat it effectively.[11,12]

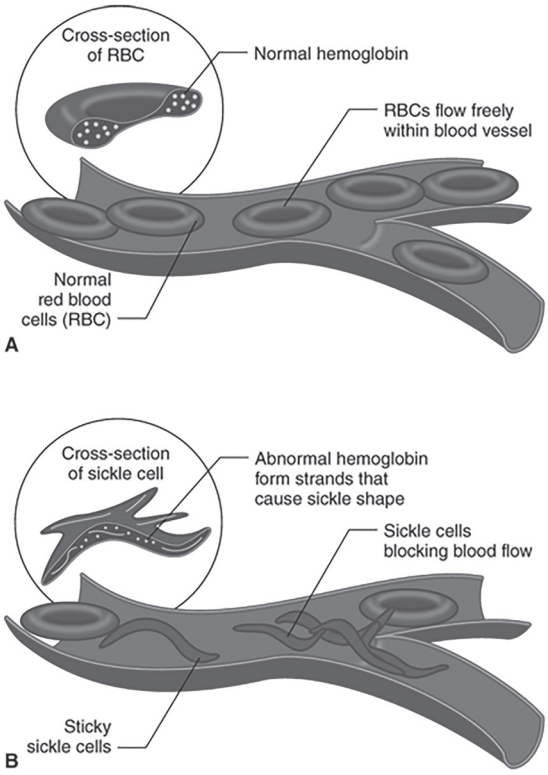
The mainstay of treatment from the perspective of the emergency practitioner in patients who present with vaso-occlusive crisis includes hydration, pain control, and nonpharmacologic interventions such as heat and distraction. No specific hydration treatment has been found to be more beneficial than another, but oral fluids are a reasonable approach if the patient is well-appearing and has no signs of significant volume loss on physical exam.[13] In patients with advanced disease, impaired renal function may contribute to dehydration, and in patients with fever or vomiting, intravenous (IV) rehydration may be necessary. It is important to keep in mind that overhydration may lead to atelectasis and acute chest syndrome.[13] In addition, overuse of crystalloids can cause a hyperchloremic metabolic acidosis, which in turn promotes sickling and can worsen patients' symptoms.[14] Finally, the combination of opioids and IV fluid boluses has been shown to increase vascular permeability and pulmonary edema.[14] For these reasons, large fluid boluses should be avoided unless clinically indicated (such as hypotension), and fluids plus oral intake should not exceed 1-1.5 times maintenance.[14]

As mentioned earlier, patients who present with sickle cell pain likely already have attempted to achieve pain control at home before coming to the ED, and most have had vaso-occlusive crises previously. In addition, some adults with sickle cell disease take daily high-dose oral opioids as prescribed by their primary care provider or hematologist. For this reason, starting with IV opioids, such as morphine or hydromorphone, is not unreasonable. These patients usually have significant pain, so multiple doses likely will be needed to achieve pain control. Rapid administration of pain medications is recommended.

For adults with sickle cell disease, morphine 8 to 12 mg IV or hydromorphone 1 to 2 mg IV may be used,[14] and may be increased by 25% and repeated twice every 15 to 30 minutes to provide pain relief.[1] Recently, studies in children with sickle cell disease suggest that intranasal fentanyl as the initial medication, followed by IV opioids, may be effective in achieving pain control and may increase rates of discharge.[15] If the patient's pain is not well controlled after multiple modalities of pain control are attempted in the ED, admission for continued IV opioids may be warranted. In areas with large populations of patients with sickle cell disease, many EDs have developed standardized order sets or protocols for pain control. This assists with patient expectations and ensures a timely disposition.

The National Institutes of Health has developed an algorithm to help practitioners guide their management.[1] (*See Figure 2.*) Nonpharmacologic interventions include applying heat packs to painful areas, creating a relaxing atmosphere (as possible), and providing distractions such as TV or handheld devices.

## Figure 1. Normal Red Blood Cells vs. Sickle Cells

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Other novel approaches to vaso-occlusive crisis recently have emerged in the literature, including low-dose ketamine, tinzaparin, clotrimazole, magnesium, erythropoietin, butyric acid, and azacitidine. The authors of a study published in 2017 did not find a reduction in severity of painful crisis or length of hospital stay while using oral or IV magnesium.[16] In a 2004 study, purified poloaxmer 188 showed promise, causing reduction in pain in vaso-occlusive crisis,[17] but a larger study did not show benefit.[18] Hydroxyurea is effective for long-term prevention of sickle cell-related complications and improves survival by blocking DNA synthesis, impairing cell division, and increasing levels of HbF. Hydroxyurea reduces both frequency and severity of attacks, but is not recommended as treatment in acute crises as it usually takes weeks to months to achieve effectiveness.[19,20,21]

Researchers in current ongoing clinical trials are in the process of developing treatments for vaso-occlusive crisis that may be of benefit in the future. Rivipansel (GMI-1070) is a therapy currently in Phase III clinical trials. It is a pan-selectin inhibitor, which blocks the activity of selectins. These molecules are responsible for blood cell adhesion. In Phase II of the trial, large reductions in time to resolution of pain crisis and length of hospital stay were seen.[22]

Researchers have studied anticoagulation and antioxidants as a means to prevent pain crises with agents such as platelet inhibitors (prasugrel and ticlopidine), vitamin K antagonists (acenocoumarol), and *N*-acetylcysteine. None of these treatments were found to be significantly effective in their trials.[23]

## Bone Necrosis

As stated earlier, the diagnosis of vaso-occlusive crisis usually is clinical. If the patient's pain is localized to the hip or shoulder, this may suggest aseptic necrosis of the femoral head, and radiographs may be obtained. This is seen most commonly in the femoral heads, where chronic weight bearing contributes to progressive joint destruction from frequent infarction of bone trabeculae.[24] Osteomyelitis and osteonecrosis may be visualized on X-ray, but magnetic resonance imaging (MRI) or bone scan is needed to detect small bone infarcts.[25]

## Acute Chest Syndrome

Acute chest syndrome is one of the most feared complications of sickle cell disease and carries a mortality rate of 10%.[26] It is commonly seen in children and is the leading cause of death in sickle cell patients in the United States.[27] It is defined as the appearance of a new infiltrate on chest X-ray accompanied by a fever > 38.5° C or respiratory symptoms such as coughing, wheezing, tachypnea, or chest pain.[28]

Although the pathophysiology is not completely understood, acute chest syndrome is thought to be caused by various etiologies, including underlying pulmonary infection (common causes include *Mycoplasma*, *Chlamydia*, and *Streptococcus*[26]) or rib infarction.[29,30] (*See Figure 3.*) Although less common, fat emboli also have been shown to cause acute chest syndrome, especially in adults with sickle cell disease. The pathophysiology involves an extension from vaso-occlusive crisis in which necrotic bone fragments embolize into the pulmonary vasculature. This has been noted on lung tissue biopsy where fat droplets are detected in endothelial cells, and on autopsy where bone fragments and marrow are found in the vasculature.[31] When ischemia and hypoxia develop in lung tissue, free radicals develop, which causes upregulation of endothelial adhesion molecules.[32] This in turn causes binding of sickled erythrocytes, thereby worsening occlusion. This cycle is thought to be responsible for causing acute chest syndrome. As previously stated, it also can be precipitated iatrogenically by overcorrecting fluid deficits in pain crisis, causing pulmonary edema.

A chest X-ray should be ordered in all patients presenting with the aforementioned symptoms, although it is important to note that imaging studies initially may be normal, so treatment should be guided based on the patient's symptoms and physical exam.[28] Once the diagnosis is made, patients are hospitalized and

treated with broad-spectrum antibiotics with coverage for community-acquired pneumonia, most commonly azithromycin and ceftriaxone to cover atypical and bacterial organisms.[26] Testing for influenza and treatment with antivirals if results are positive also are recommended. Bronchospasm may be present, so inhaled beta-2 adrenergic agonists may be tried.[33] Systemic steroids are not recommended, as they were associated with increased rates of readmission within 72 hours for vaso-occlusive pain.[14] Researchers in one study found no benefit from early inhaled corticosteroid therapy.[34]

Supportive measures, including oxygen, IV fluids, and pain control, should be provided as needed. It is estimated that about 13% of patients with acute chest syndrome will require ventilator support.[6]

In addition, treatment of acute chest syndrome generally includes transfusion. Transfusion therapy is thought to be lifesaving by many practitioners, but currently there is no evidence-based research to back this theory. It is effective by decreasing the concentration of sickled hemoglobin in the body. The decision of whether to use simple or exchange transfusion depends on the severity of the episode. It is recommended to consider the use of simple transfusion for milder cases of acute chest syndrome and exchange transfusion in moderate to severe episodes.[26] While some researchers recommend transfusion in all patients who present with acute chest syndrome, it should be considered in the following populations: those who have a previous history of intubation, those who deteriorate despite other therapies, and those with suspected fat embolism.[29,30]

Another treatment is inhaled nitric oxide, which causes vasodilation and improves ventilation and perfusion in areas of damaged lung tissue.[29] It also reduces adhesion of red blood cells to endothelial cells, but its effectiveness is controversial. In a study published in 2015, researchers found no reduction in rates of treatment failure in adult patients with mild to moderate acute chest syndrome treated with nitric oxide.[35] Unfortunately, acute chest syndrome may occur multiple times in patients with sickle cell disease, predisposing them to chronic lung disease.[36]

## Splenic Sequestration Crisis

Splenic sequestration crisis is a phenomenon seen in sickle cell disease patients in which there is an acute drop in hemoglobin due to vaso-occlusion combined with an increase in organ size due to pooling of red blood cells inside the spleen. It is seen most commonly in children with sickle cell anemia (HbSS).[37] This sequestration can cause a large amount of intravascular volume loss, which ultimately can lead to hypovolemic shock.[37] On physical exam, the patient will be tachycardic, appear pale, and have a palpable spleen. Pain in the left upper quadrant frequently is seen, but is not necessary for the diagnosis. Laboratory results show a hemoglobin level well below baseline as well as a normal to increased reticulocyte count.

With a mortality rate between 10% and 15%, it is crucial that treatment is started early.[38] Therapy includes aggressive IV fluid hydration for hypotension and blood transfusion. This restores intravascular volume and also aids in remobilizing red blood cells (RBCs) in the spleen, producing a rise in hemoglobin greater than what would be seen with transfusion alone.[39,40] Providers should consult a sickle cell disease expert during the treatment phase of splenic sequestration, as rapid increases in blood viscosity may cause stroke or acute chest syndrome. All patients should be admitted to a monitored bed with frequent hemoglobin checks and neurologic examinations. In patients with recurrent sequestration or symptomatic hypersplenism, splenectomy often is required.[39]

## Hyperhemolytic Crisis

Patients with sickle cell disease have a chronic hemolytic anemia due to the abnormal shape of the red blood cells. Patients generally have a baseline hemoglobin of 6-9 g/dL and a reticulocyte count of 5-15%.[41] Although this anemia usually is compensated for by increased red blood cell production, patients can experience sudden drops in hemoglobin concentration due to a variety of factors, including stress, infection, or medications. Patients usually will present to the ED complaining of weakness, fatigue, or exertional dyspnea. One specific entity is known as hyperhemolytic crisis, which is defined as a decrease in hemoglobin concentration with normal or increased reticulocyte count.[42] Transfusion is the first-line therapy, but other treatments, such as intravenous immunoglobulin (IVIG) and steroids, have been used.[43]

## Aplastic Crisis

Aplastic crisis occurs when there is a decrease in hemoglobin greater than 2 g/dL below baseline coupled with an absent compensatory mechanism in the bone marrow, leading to a critically low reticulocyte count. It occurs most commonly in children and is associated with parvovirus B19 infection.[41] Symptoms typically include weakness, fatigue, tachycardia, and pallor. The episode usually is self-limiting and resolves in two days to two weeks. Treatment involves supportive care and transfusion in moderate to severe cases until natural erythropoiesis is restored.[44] Most patients are admitted for close monitoring.

## Stroke

Although an uncommon complication overall, stroke in sickle cell disease is one of the most devastating. Children with sickle cell disease have a 200% greater likelihood of experiencing a cerebrovascular accident than those without the disease.[45] Unfortunately, there are no prospective studies regarding stroke evaluation and management in sickle cell disease patients, so guidelines are based on recommendations from expert consensus. Stroke in sickle cell disease typically occurs in children younger than 10 years of age and in adults older than 29 years of age.[46] Children and older adults with sickle cell disease typically have ischemic stroke; hemorrhagic strokes are common beginning in the third decade of life.[46] Because the pathophysiology behind strokes in children and adults with sickle cell disease differs, the evaluation and management must be considered separately. As with vaso-occlusion crisis, children who present to the ED with signs and symptoms of stroke have underlying inappropriate cell adhesion and intravascular sickling.[14] In adults,

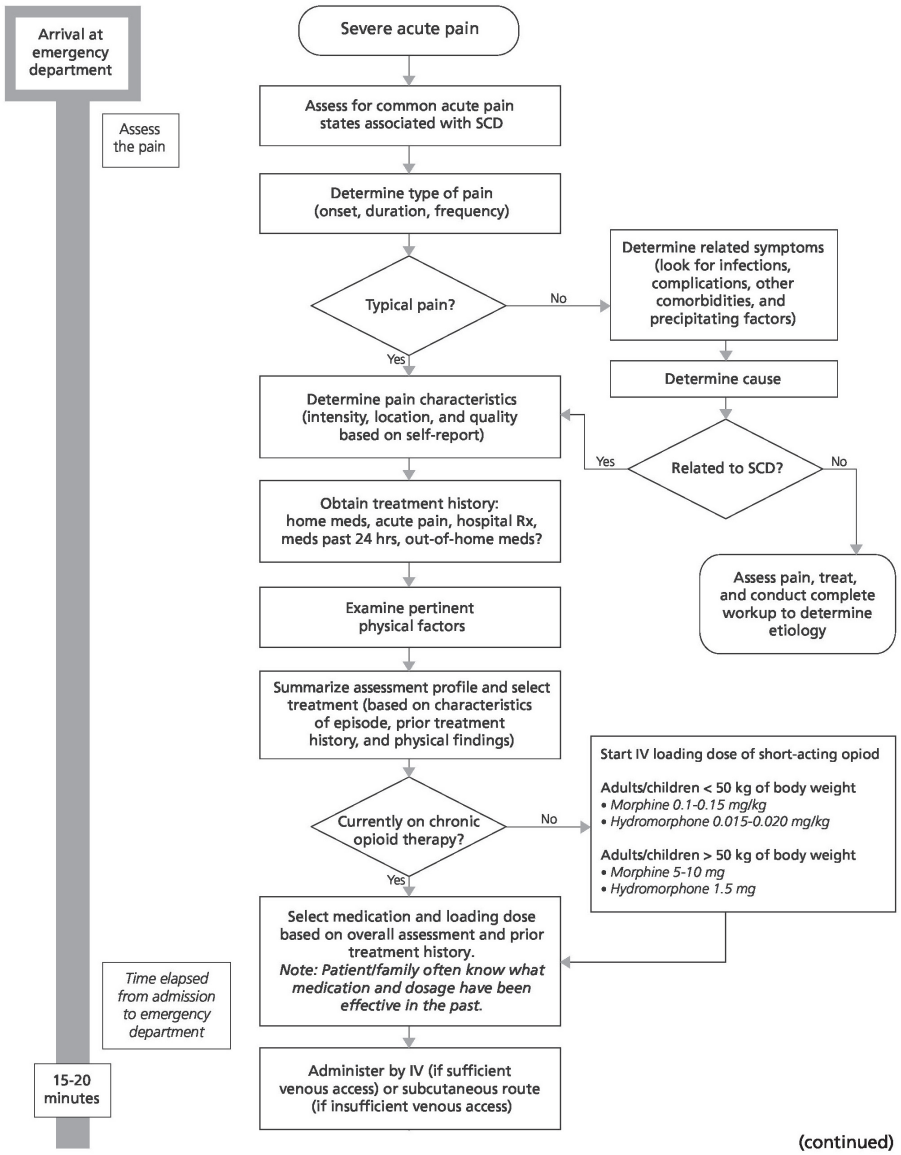
the cause usually is a thromboembolic event, just as is seen in the general population. A careful and detailed neurologic exam is required, and the provider should question the time of onset.

Clinical presentation and neurologic deficits will depend on the anatomic area of the brain affected. These patients need to undergo emergent noncontrast head CT with or without perfusion studies, followed by MRI and magnetic resonance angiography (MRA) of the head and neck.

Children with ischemic strokes typically are treated with IV fluids and exchange transfusion to maintain an HbS level less than 30%.[46] These patients should be transfused with caution, as post-transfusion hemoglobin levels greater than 13 g/dL have been associated with additional ischemia secondary to hyperviscosity.[46] Hemorrhagic conversion is common in children,[47] and unfortunately no studies regarding management in sickle cell disease have been published. Because of this, it is recommended to treat children presenting with hemorrhagic strokes according to guidelines created for non-sickle cell disease patients.[47] Adults presenting with ischemic strokes should undergo evaluation for potential tissue plasminogen activator (tPA) or intra-arterial thromoblysis candidacy in conjunction with a stroke neurologist and hematologist.[14]

Because of the high recurrence rates following an initial stroke, experts recommend patients be placed on chronic transfusion therapy, which can reduce the risk of subsequent stroke by up to 92%.[48] In one retrospective cohort study, exchange transfusion was associated with lower rates of recurrent strokes when compared to simple transfusion therapy.[49] In addition, randomized controlled trials suggest that annual transcranial Doppler studies be performed on children with sickle cell disease between 2 and 16 years of age to detect signs of cerebrovascular disease. In patients with a Doppler velocity greater than 200 cm/s, prophylactic chronic transfusion therapy is recommended.[50]

## Figure 2. ED Evaluation and Treatment



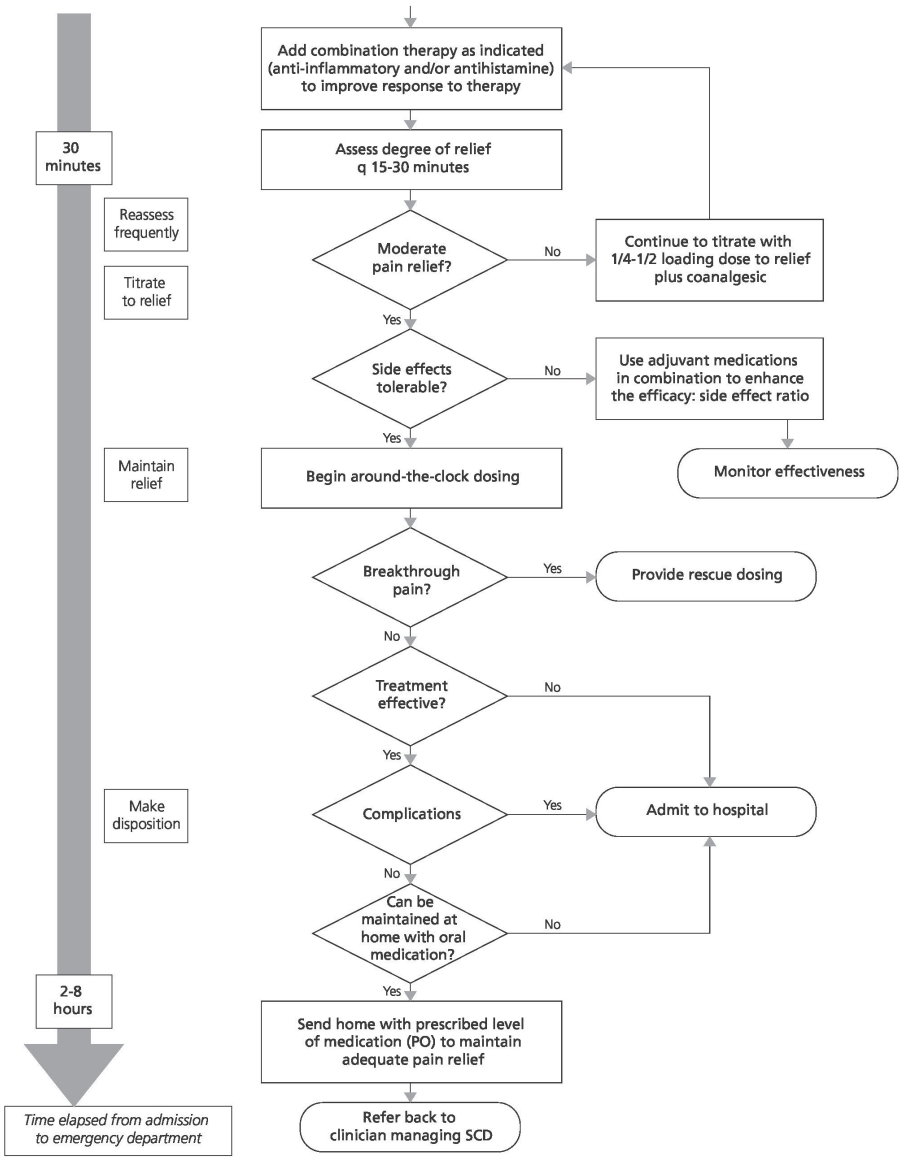

Source: National Institutes of Health, National Heart, Lung, and Blood Institute. *The Management of Sickle Cell Disease*. 4th edition. NIH publication no. 02-2117. Bethesda, MD: 2002: 66-67.

## Infection

Patients with sickle cell disease have an increased risk of infection due to the development of functional asplenia in childhood, predisposing them to infection, especially with encapsulated or atypical organisms,[51] such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma*, and *Chlamydophilia pneumoniae*.[52] Because of recent widespread vaccination against *S. pneumoniae* and *H. influenzae*, infection with these organisms has declined significantly. However, patients with sickle cell disease have an immunocompromized state, as they experience increased bone marrow turnover and abnormal complement activation.[14] Therefore, any patient with sickle cell disease who presents to the ED with a fever within 24 hours of presentation or other signs of infection should be treated aggressively.

Causes of fever in this population include bacteremia/sepsis and infection with acute chest syndrome, and less commonly, osteomyelitis and meningitis. As with any patient presenting with signs and symptoms of infection, a thorough history and physical exam should be performed to determine the source of infection. If no source is evident, the

## Figure 2. ED Evaluation and Treatment (continued)




Source: National Institutes of Health, National Heart, Lung, and Blood Institute. *The Management of Sickle Cell Disease*. 4th edition. NIH publication no. 02-2117. Bethesda, MD: 2002: 66-67.

provider should perform a complete blood count and blood cultures, and consider obtaining urinalysis and urine culture in children younger than 2 years of age. Specific diagnostic laboratory tests to be considered, based on history and physical exam, may include throat culture, chest radiograph, lumbar puncture for toxic-appearing patients, and analyses and cultures of subperiosteal fluid aspiration or arthrocentesis.[53]

Treatment consists of antibiotics, and specific therapy should be based on the identified source of infection. Treat empirically with a third-generation cephalosporin, such as ceftriaxone (2 g in adults and 50 mg/kg in children) to cover the typical organisms seen.[14] Patients with suspicion for significant bacterial infection should be considered for admission. Some patients may be sent home in certain scenarios. In children who are well-appearing with a temperature less than 40° C, who are at their baseline lab values, and who have good follow-up care may be discharged after a single dose of long-acting antibiotic therapy.[53] In terms of prophylaxis, the use of daily penicillin V has been shown to reduce the incidence of infection and mortality from sepsis in children 2 months to 5 years of age but not in adults.[14,54]

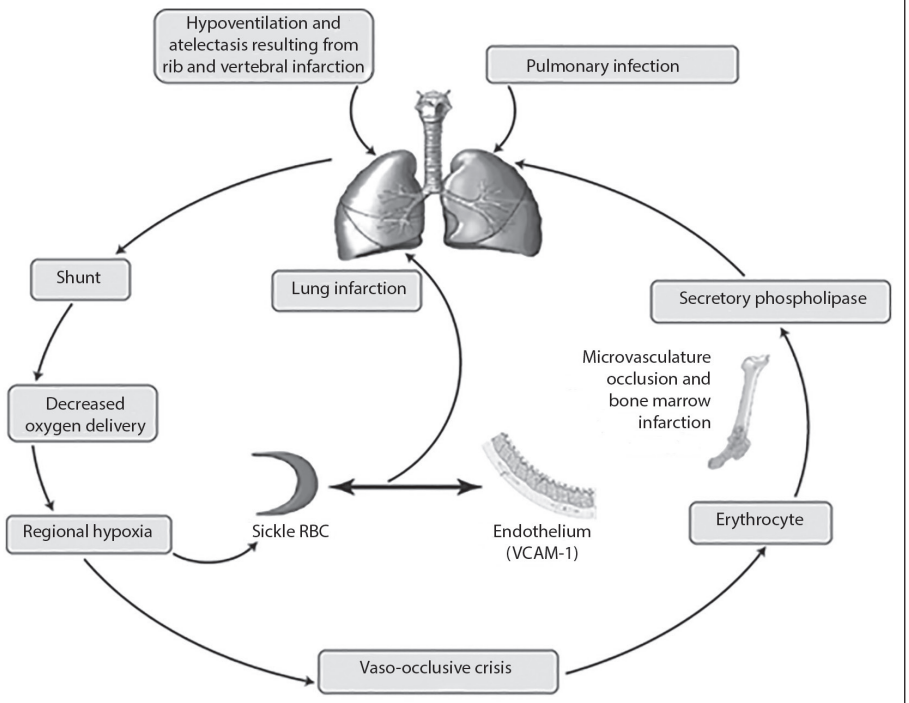
In patients with fever who are complaining of bone pain, providers should consider osteomyelitis and septic arthritis. Sites of infarcted bone due to previous episodes of recurrent vaso-occlusive crisis have an increased susceptibility for infection.[54] It is usually due to infection with *Streptococcus* or *Staphylococcus* species, but antibiotic coverage should include *Salmonella* species.[55] Findings concerning for septic arthritis or osteomyelitis include joint swelling, warmth, and tenderness. Patients are likely to have severe pain upon passive range of motion of the joint in septic arthritis. Optimal diagnostic studies remain unclear, as plain films may fail to show changes associated with bone destruction until seven to 10 days after onset.[56] While MRI may be the most helpful noninvasive diagnostic study in sickle cell disease joint infections, bone biopsy and joint aspiration are the gold standard modalities in osteomyelitis and septic arthritis, respectively.[57]

## Cardiac Complications

Chronic sickling and frequent microinfarcts can lead to cardiac dysfunction over time.[58] Cardiomegaly is seen commonly in sickle cell disease patients, and it correlates with the degree of chronic anemia.[59] Patients with sickle cell disease are at increased risk for myocardial infarction, QT prolongation, atrioventricular blocks, and ventricular arrhythmias.[60,61] In an autopsy study in 1996 of 72 patients with sickle cell disease, seven were found to have pathologic evidence of previous myocardial infarction (MI) but without signs of atherosclerotic lesions.[62] There are no studies that provide recommendations of troponin use in young sickle cell disease patients who present to the ED with chest pain without coronary artery disease risk factors. Therefore, cardiac enzymes should be ordered at the provider's discretion.

Rarely, sickle cell trait has been shown to increase the risk of sudden cardiac death during intense physical activity, which leads to hypoxia and acidosis. In turn, this promotes sickling, vascular occlusion, and acute increases in

## Figure 3. Acute Chest Syndrome

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pulmonary pressures.[59,63] This was seen in 2008, when controversy surrounded a University of Central Florida football player with sickle cell trait who died suddenly during an intense practice session. A statistical review published in 2012 found that over a 31-year span, out of 2,462 athlete deaths, 23 were related to sickle cell disease.[64] Evidence-based guidelines still are lacking for measures to prevent sudden cardiac death in sickle cell disease patients. Further studies are needed to identify cardiac risk factors associated with increased mortality. Once established, this subset of high-risk patients can be followed more closely and possible lifesaving interventions can be made to reduce the risk of premature cardiac death.[64]

## Pulmonary Embolism

Sickle cell disease has been shown to increase the risk of pulmonary embolism (PE) because of its hypercoagulable state. In a study of patients with a history of sickle cell disease and sudden death, 38% were found to have a PE at the time of autopsy.[65] Data from the National Hospital Discharge Survey showed patients hospitalized with sickle cell disease were three times as likely to be discharged with a diagnosis of PE as those without the disease.[66] Patients typically will present with dyspnea, chest pain, hypoxia, tachycardia; lower extremity swelling and pain often are absent. As split product levels are increased at baseline in patients with sickle cell disease, D-dimer is of little use.[67] No studies have shown optimal therapy for the treatment of PE in patients with sickle cell disease. Therefore, it is recommended that these patients be treated with the same therapy as patients without the disease.[68]

## Priapism

Priapism is a phenomenon in which there is sustained penile erection in the absence of sexual desire. It is seen in patients both with and without sickle cell disease,[14] but it is a common complaint seen in patients with sickle cell disease. Priapism is thought to occur in as many as 35% of males with sickle cell disease.[69] The condition is categorized as low flow or high flow. The low-flow state is ischemic and is more common in sickle cell disease patients, while the high-flow state is non-ischemic. Patients with sickle cell disease often have multiple occurrences of priapism, which can lead to erectile dysfunction over time.

The risk of priapism in sickle cell disease is thought to stem from a decrease in circulating free nitric oxide.[70] Patients with sickle cell disease undergo chronic hemolysis, which increases the ability of free hemoglobin to bind nitric oxide.[70] Priapism is a form of compartment syndrome in which there is an acute increase in pressure in the venous sinuses, which in turn leads to decreased penile arterial flow. As with any other ischemic process, timely diagnosis and treatment is of critical importance, as prolonged episodes of priapism can lead to permanent tissue damage.

Patients with priapism will present with a rigid, painful corpus cavernosa. The provider should inquire about possible triggers, including trauma, dehydration, stress, infection, or drugs such as cocaine or phosphodiesterase inhibitors like sildenafil.[14]

If the erection has been present for two hours or less, the patient should be given IV fluids and oral analgesia to see if the priapism resolves on its own. If the duration is longer, the provider may attempt to aspirate and irrigate the corpus cavernosum.[71] A penile block may be performed for patient comfort. Once anesthetized, two small needles may be inserted into each corporal body. Aspiration of blood alone may result in complete resolution. If the erection remains, an alpha-adrenergic agonist, such as phenylephrine, may be injected into the opposite needle.[14,70,71] The phenylephrine may be diluted to 100 to 500 mcg/mL and injected as 0.5 to 1 mL every five minutes for a total of three times.[72] Penile aspiration should occur within six hours of the onset of priapism, as irreversible tissue necrosis can occur.[71] If this is unsuccessful, exchange transfusion can be considered in consultation with urology and hematology.[14] If aspiration and irrigation do not provide detumescence, urology may be consulted for surgical shunt placement.[71] If the provider is successful in relieving the priapism, the penis should be wrapped to prevent re-accumulation of blood. Patients may be discharged

home with close urology follow-up. Other potential intracorporal agents, such as etilefrine, have been studied, but currently are not available in the United States.[71]

## Hyphema

A hyphema occurs when blood enters the anterior chamber, either spontaneously or as a result of trauma to the eye. In the setting of trauma, force causes rupture of an iris root vessel.[73] The presence of sickle cell disease or sickle cell trait can lead to complications following development of a hyphema. These include rebleeding and increases in intraocular pressure leading to acute angle closure glaucoma. A full eye exam should be performed. This includes visual acuity, visual field testing, fundoscopic exam, slit-lamp exam, intraocular pressure measurement, and fluorescein staining.

Patients with a confirmed hyphema should have the head of the bead raised to 45 degrees. This promotes settling of the RBCs and prevents occlusion of the trabecular meshwork, which can elevate intraocular pressure.[14] If the pressure is found to be elevated above 20 mmHg, treatment consists of topical beta-blockers, such as timolol, and alpha-adrenergic agonists like apraclonidine.[73] Carbonic anhydrase inhibitors, such as acetazolamide, should be avoided in patients with sickle cell disease, as they cause a drop in the anterior chamber pH, which promotes sickling and worsening of intraocular pressure.[73] Another agent traditionally used in hyphema, mannitol, also should be avoided in sickle cell disease, as it can cause an increase in serum osmolality.[14] An ophthalmologist should be consulted, and these patients should be admitted for serial intraocular pressure exams, as any increase above normal may require surgical anterior chamber washout.[73]

## Differential Diagnosis

Sickle cell disease can affect almost any organ in the body. For this reason, the differential diagnosis for patients presenting with symptoms of sickle cell complications is extremely broad. Pain is the most common complaint in patients with sickle cell disease seen in the ED. Many providers initially may assume the patient's symptoms are due to vaso-occlusive crisis. However, it is important to remember that this disease entity is a diagnosis of exclusion, and one must rule out other serious causes of pain before making the diagnosis.

## Long-term Management and Treatment

Patients with sickle cell disease need to maintain close follow-up with an outpatient provider knowledgeable about sickle cell disease. Sickle cell patients can be divided into two groups: high ED utilizers and low ED utilizers. About 20% are considered high utilizers and make up the majority of the population seen in the ED. These patients should be referred to a hematologist or outpatient provider with a specific background in sickle cell disease to ensure the highest quality of care. If the patient does not have a current provider, consider engaging case management or referring the patient to the Sickle Cell Disease Association of America, which will assist the patient in their search. Because the ED sees a disproportionate number of high utilizers, it is important not to assume all patients with sickle cell disease are high utilizers or drug seekers.

While there are various ways to manage sickle cell disease effectively, bone marrow transplant (BMT) may be curative. The data on survival rates after BMT are limited, as current patient eligibility in the United States is dependent on the presence of pulmonary and neurologic vasculopathies. Published data regarding HLA-matched sibling BMT estimates overall survival rates greater than 90% at four to six years.[74] Gene therapy is a new approach that currently is under investigation for the treatment and potentially a cure for the disease. CRISPR is a gene-editing tool that stands for clustered regularly interspaced palindromic repeats, which uses nuclease to slice DNA segments. By doing this, CRISPR potentially could delete the mutated sequence seen in sickle cell disease. One specific CRISPR, called Cas9, was found to correct 30% of the β-hemoglobin DNA sequence.[75] Studies are promising but still ongoing.

## Controversies

Medical advances are changing our outlook and knowledge of sickle cell disease, so many prior papers regarding its management now are obsolete. In addition, sickle cell disease is underfunded in comparison with other disorders. There is a lack of research and funding. As an example, cystic fibrosis receives 11 times the amount of monetary support per patient than sickle cell disease.[76] Sickle cell disease also is a relatively rare disease, making clinical trials difficult to perform. This lack of funding and research has caused controversy in the sickle cell community. Many advocates believe the shortage stems from the fact that the disease primarily affects African Americans, and that racial discrimination and lack of wealth in the community play a role.

## Summary

Sickle cell disease can present a variety of challenges to the ED provider. It is a disease with many complications that may be missed easily if not carefully considered and evaluated. With new research and innovative ways of treating the disease being developed, the idea that patients with sickle cell disease may be managed with more effective disease-modifying therapies, thereby reducing their need for ED care, is becoming a reality.

## References


1. Yawn BP, John-Sowah J. Management of sickle cell disease: Recommendations from the 2014 Expert Panel Report. *Am Fam Physician* 2015;92:1069-1076.
2. Angastiniotis M, Modell B, Englezos P, Boulyjenkov V. Prevention and control of haemoglobinopathies. *Bull World Health Organ* 1995;73:375-386.
3. Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: A HuGE review. *Am J Epidemiol* 2000;151:839-845.
4. Aliyu ZY, Tumblin AR, Kato GJ. Current therapy of sickle cell disease. *Haematologica* 2006;91:7-10.
5. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw Hill; 2016:1505-1506.
6. Marx JA, Hockberger R, Walls R. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 8th ed. Philadelphia: Saunders; 2014:1596-1597.
7. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive*

*Study Guide*. 8th ed. New York: McGraw Hill; 2016:955.
8. Ernst AA, Weiss SJ, Johnson WD, Takakuwa KM. Blood pressure in acute vaso-occlusive crises of sickle cell disease. *South Med J* 2000;93:590-592.
9. Aisiku IP, Smith WR, McClish DK, et al. Comparisons of high versus low emergency department utilizers in sickle cell disease. *Ann Emerg Med* 2009;53:587-593.
10. Morrison AK, Myrvik MP, Brousseau DC, et al. Parents' pain medication underdosing is associated with more emergency department visits in sickle cell disease. *Pediatric Blood Cancer* 2018 Apr;65(4).
11. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Ann Emerg Med* 2001;38:633-638.
12. Garra G, Singer AJ, Taira BR, et al. Validation of the Wong-Baker FACES Pain Rating Scale in pediatric emergency department patients. *Acad Emerg Med* 2010;17:50-54.
13. Cecchini J, Fartoukh M. Sickle cell disease in the ICU. *Curr Opin Crit Care* 2015;21:569-575.
14. Glassberg J. Evidence-based management of sickle cell disease in the emergency department. *Emerg Med Pract* 2011;13: 1-20.
15. Kavanagh PL, Sprinz PG, Wolfgang TL, et al. Improving the management of vaso-occlusive episodes in the pediatric emergency department. *Pediatrics* 2015;136:e1016-25.
16. Than NN, Soe HHK, Palaniappan SK, et al. Magnesium for treating sickle cell disease. *Cochrane Database Syst Rev* 2017;4:CD011358.
17. Gibbs WJ, Hagemann TM. Purified poloxamer 188 for sickle cell vaso-occlusive crisis. *Ann Pharmacother* 2004;38: 320-324.
18. Danielson CF. The role of red blood cell exchange transfusion in the treatment and prevention of complications of sickle cell disease. *Ther Apher* 2002;6:24-31.
19. 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.
20. Darbari DS, Panepinto JA. What is the evidence that hydroxyurea improves health-related quality of life in patients with sickle cell disease? *Hematology Am Soc Hematol Educ Program* 2012;2012:290-291.
21. Ware RE. How I use hydroxyurea to treat young patients with sickle cell anemia. *Blood* 2010;115:5300-5311.
22. Telen MJ, Wun T, McCavit TL, et al. Randomized phase 2 study of GMI-1070 in SCD: Reduction in time to resolution of vaso-occlusive events and decreased opioid use. *Blood* 2015;125:2656-2664.
23. Sins JWR, Mager DJ, Davis SCAT, et al. Pharmacotherapeutical strategies in the prevention of acute, vaso-occlusive pain in sickle cell disease: A systematic review. *Blood Adv* 2017;1:1598-1616.
24. Adesina O, Brunson A, Keegan THM, Wun T. Osteonecrosis of the femoral head in sickle cell disease: Prevalence, comorbidities, and surgical outcomes in California. *Blood Adv* 2017;1:1287-1295.
25. Mont MA, Marulanda GA, Jones LC, et al. Systematic analysis of classification systems for osteonecrosis of the femoral head. *J Bone Joint Surg Am* 2006;88(Suppl 3): 16-26.
26. Vichinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. *N Engl J Med* 2000;342:1855-1865.
27. Platt OS. The acute chest syndrome of sickle cell disease. *N Engl J Med* 2000;342:1904-1907.
28. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw Hill; 2016:1507-1508.
29. Paul RN, Castro OL, Aggarwal A, Oneal PA. Acute chest syndrome: Sickle cell disease. *Eur J Haematol* 2011;87:191-207.
30. Desai PC, Ataga KI. The acute chest syndrome of sickle cell disease. *Expert Opin Pharmacother* 2013;14:991-999.
31. Styles LA, Aarsman AJ, Vichinsky EP, Kuypers FA. Secretory phospholipase A(2) predicts impending acute chest syndrome in sickle cell disease. *Blood* 2000;96: 3276-3278.
32. Klings ES, Farber HW. Role of free radicals in the pathogenesis of acute chest syndrome in sickle cell disease. *Respir Res* 2001;2:280-285.
33. Knight-Madden JM, Hambleton IR. Inhaled bronchodilators for acute chest syndrome in people with sickle cell disease. *Cochrane Database Syst Rev* 2012;7:CD003733.
34. Leonard A, Godiwala N, Herrera N, et al. Early initiation of inhaled corticosteroids does not decrease acute chest syndrome morbidity in pediatric patients with sickle cell disease. *Blood Cells Mol Dis* 2018. doi: 10.1016/j.bcmd.2018.03.001. [Epub ahead of print].
35. Maitre B, Djbre M, Katsahian S, Habibi A. Inhaled nitric oxide for acute chest syndrome in adult sickle cell patients: A randomized controlled study. *Intensive Care Med* 2015;41:2121-2129.
36. Powars D, Weidman JA, Odom-Maryon T, et al. Sickle cell chronic lung disease: Prior morbidity and the risk of pulmonary failure. *Medicine* 1988;67:66-76.
37. Pappo A, Buchanan GR. Acute splenic sequestration in a 2-month-old infant with sickle cell anemia. *Pediatrics* 1989;84: 578-579.
38. Emond AM, Collis R, Darvill D, et al. Acute splenic sequestration in homozygous sickle cell disease: Natural history and management. *J Pediatr* 1985;107:201-206.
39. Jenkins TL. Sickle cell anemia in the pediatric intensive care unit: Novel approaches for managing life-threatening complications. *AACN Clin Issues* 2002;13:154-168.
40. Grover R, Wethers DL. Management of acute splenic sequestration crisis in sickle cell disease. *J Assoc Acad Minor Phys* 1990;1:67-70.
41. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw Hill; 2016:1509.
42. Gouveia ME, Soares NB, Santoro MS, de Azevedo FC. Hyperhemolysis syndrome in a patient with sickle cell anemia: Case report. *Rev Bras Hematol Hemoter* 2015;37:266-268.
43. Cullis JO, Win N, Dudley JM, Kaye T. Post-transfusion hyperhaemolysis in a patient with sickle cell disease: Use of steroids and intravenous immunoglobulin to prevent further red cell destruction. *Vox Sang* 1995;69:355-357.
44. Jenkins TL. Sickle cell anemia in the pediatric intensive care unit: Novel approaches for managing life-threatening complications. *AACN Clin Issues* 2002;13:154-168.
45. Lei H, Juan AH, Kim MS, Ruddle FH. Identification of a Hoxc8-regulated transcriptional network in mouse embryo fibroblast cells. *Proc Natl Acad Sci U S A* 2006;103:10305-10309.
46. Ohene-Frempong K, Weiner SJ, Sleeper LA. Cerebrovascular accidents in sickle cell disease: Rates and risk factors. *Blood* 1998;91:288-294.
47. Elbers J, Wainwright MS, Amlie-Lefond C. The Pediatric Stroke Code: Early management of the child with stroke. *J Pediatr* 2015;167:19-24.e1-4.
48. Adams RJ. Stroke prevention and treatment in sickle cell disease. *Arch Neurol* 2001;58:565-568.
49. Hulbert ML, Scothorn DJ, Panepinto JA. Exchange blood transfusion compared with simple transfusion for first overt stroke is associated with a lower risk of subsequent stroke: A retrospective cohort study of 137 children with sickle cell anemia. *J Pediatr* 2006;149:710-712.
50. 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.
51. Ramakrishnan M, Moïsi JC, Klugman KP, et al. Increased risk of invasive bacterial infections in African people with sickle-cell disease: A systematic review and meta-analysis. *Lancet Infect Dis* 2010;10:329-337.
52. Sobota A, Sabharwal V, Fonebi G, Steinberg M. How we prevent and man-

age infection in sickle cell disease. *Br J Haematol* 2015;170:757-767.
53. National Institutes of Health. National Heart, Lung and Blood Institute. *The Management of Sickle Cell Disease*. 4th ed. NIH Publication No. 02-2117. Bethesda, MD: NIH; 2002:77-78.
54. Bennett OM, Namnyak SS. Bone and joint manifestations of sickle cell anaemia. *J Bone Joint Surg Br* 1990;72:494-499.
55. Anand AJ, Glatt AE. Salmonella osteomyelitis and arthritis in sickle cell disease. *Semin Arthritis Rheum* 1994;24:211-221.
56. Rao S, Solomon N, Miller S, Dunn E. Scintigraphic differentiation of bone infarction from osteomyelitis in children with sickle cell disease. *J Pediatr* 1985;107:685-688.
57. Chambers JB, Forsythe DA, Bertrand SL, et al. Retrospective review of osteoarticular infections in a pediatric sickle cell age group. *J Pediatr Orthop* 2000;20:682-685.
58. Voskaridou E, Christoulas D, Terpos E. Sickle-cell disease and the heart: Review of the current literature. *Br J Haematol* 2012;157:664-673.
59. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw Hill; 2016:1510.
60. Gladwin MT, Sachdev V. Cardiovascular abnormalities in sickle cell disease. *J Am Coll Cardiol* 2012;59:1123-1133.
61. Ogunbayo GO, Misumida N, Olorunfemi O, et al. Comparison of outcomes in patients having acute myocardial infarction with versus without sickle-cell anemia. *Am J Cardiol* 2017;120:1768-1771.
62. Martin CR, Johnson CS, Cobb C, et al. Myocardial infarction in sickle cell disease. *J Natl Med Assoc* 1996;88:428-432.
63. Niss O, Quinn CT, Lane A, et al. Cardiomyopathy with restrictive physiology in sickle cell disease. *JACC Cardiovasc Imaging* 2016;9:243-252.
64. Harris KM, Haas TS, Eichner ER, Maron BJ. Sickle cell trait associated with sudden death in competitive athletes. *Am J Cardiol* 2012;110:1185-1188.
65. Graham JK, Mosunjac M, Hanzlick RL, Mosunjac M. Sickle cell lung disease and sudden death: A retrospective/prospective study of 21 autopsy cases and literature review. *Am J Forensic Med Pathol* 2007;28:168-172.
66. Stein PD, Beemath A, Meyers FA, et al. Deep venous thrombosis and pulmonary embolism in hospitalized patients with sickle cell disease. *Am J Med* 2006;119:897.e7-11.
67. Naik RP, Streiff MB, Lanzkron S. Sickle cell disease and venous thromboembolism: What the anticoagulation expert needs to know. *J Thromb Thrombolysis* 2013;35:352-358.
68. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl):e419S-e496S.
69. Adeyoju AB, Olujohungbe AB, Morris J, et al. Priapism in sickle-cell disease; incidence, risk factors and complications — an international multicentre study. *BJU Int* 2002;90:898-902.
70. Olujohungbe A, Burnett AL. How I manage priapism due to sickle cell disease. *Br J Haematol* 2013;160:754-765.
71. National Institutes of Health. National Heart, Lung, and Blood Institute. *The Management of Sickle Cell Disease*, 4th ed. NIH Publication No. 02-2117. Bethesda, MD: National Institutes of Health; 2002:130-131.
72. Montague DK, Jarow J, Broderick GA, et al. American Urological Association guideline on the management of priapism. *J Urol* 2003;170(4 Pt 1):1318-1324.
73. Tintinalli JE, Stapczynski JS, Ma OJ, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*, 8th ed. New York: McGraw Hill; 2016:1566-1568.
74. Bolaños-Meade J, Brodsky RA. Blood and marrow transplantation for sickle cell disease: Overcoming barriers to success. *Curr Opin Oncol* 2009;21:158-161.
75. Mumal I. Two types of CRISPR gene editing could be useful in treating sickle cell anemia, Editas reports. *Sickle Cell Anemia News*. Available at: https://sicklecellanemianews.com/2018/02/06/editas-reports-two-types-of-crispr-gene-editing-could-be-useful-in-treating-sickle-cell-anemia. Feb. 6, 2018. Accessed April 8, 2018.
76. Smith LA, Oyeku SO, Homer C, Zuckerman B. Sickle cell disease: A question of equity and quality. *Pediatrics* 2006;117:1763-1770.

## CME/CE Questions

1. Which of the following is a known long-term complication of priapism?
   a. Penile ulcers
   b. Erectile dysfunction
   c. Paraphimosis
   d. Phimosis
2. Which of the following pain regimens is appropriate for a patient presenting in acute pain crisis?
   a. Acetaminophen 325 mg PO every five minutes
   b. Valium 2 mg PO once
   c. Fentanyl 10 mg IV every two hours
   d. Morphine 8 mg IV every 15-30 minutes
3. Patients with sickle cell disease are at increased risk for which of the following disease processes?
   a. Pulmonary embolism
   b. Appendicitis
   c. Multiple endocrine neoplasia type 2
   d. Adrenal hemorrhage
4. Which of the following is useful in the treatment of priapism in patients with sickle cell disease?
   a. Intramuscular ketorolac
   b. Injection of an alpha-adrenergic agonist into the corpus cavernosa
   c. IV ketamine
   d. Injection of cyclobenzaprine into the corpus cavernosa
5. Aplastic crisis usually is associated with which of the following in sickle cell disease?
   a. Adenovirus
   b. Parainfluenza virus
   c. Parvovirus B19
   d. Rotovirus
6. How is vaso-occlusive crisis typically diagnosed in the emergency department?
   a. CT angiography
   b. PET scan
   c. Bone scan
   d. Clinically
7. Sickle cell disease places patients at an increased risk of infection with encapsulated organisms because of its association with which of the following?
   a. Functional asplenia
   b. Leukopenia
   c. Decreased T lymphocyte stores
   d. Poor thymus function
8. Aplastic crisis typically resolves spontaneously in what time frame?
   a. Two hours
   b. Two weeks
   c. Two months
   d. Two years
9. Which of the following has been shown to be effective in prevention of vaso-occlusive crisis in patients with sickle cell disease?
   a. Tacrolimus
   b. Methotrexate
   c. Aspirin
   d. Hydroxyurea

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EMERGENCY MEDICINE REPORTS

# Sickle Cell Emergencies

| Complications of Sickle Cell Anemia | |
|---|---|
| Neurologic | Ischemic or hemorrhagic stroke<br>Cerebral aneurysm<br>Chronic pain syndrome<br>Neuropathic pain syndrome |
| Eye | Retinopathy |
| Pulmonary | Acute chest syndrome<br>Pulmonary hypertension |
| Cardiac | Cardiomegaly |
| Abdominal, GI | Mesenteric ischemia<br>Hepatic infarction<br>Cholelithiasis<br>Intrahepatic cholestasis<br>Splenic sequestration |
| Renal, GU | Hematuria<br>Renal infarction<br>Papillary necrosis<br>Renal failure<br>Priapism |
| Musculoskeletal | Acute vaso-occlusive pain crisis; bone, joint, and muscle pain<br>Osteomyelitis<br>Avascular necrosis of femoral head |
| Dermatologic | Leg ulcers |
| Infection | Osteomyelitis<br>Pneumonia<br>Urinary tract infection |
| Hematologic | Chronic hemolysis<br>Acute hemolytic crisis<br>Aplastic crisis<br>Hypercoagulability: pulmonary embolism and venous thrombosis |

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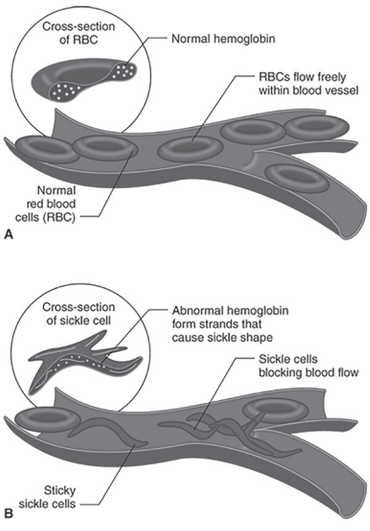
## Normal Red Blood Cells vs. Sickle Cells

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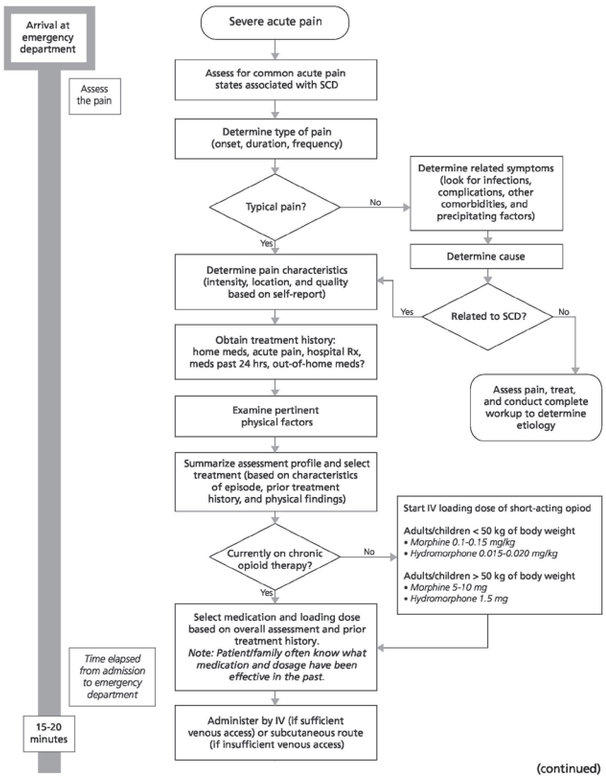
## ED Evaluation and Treatment

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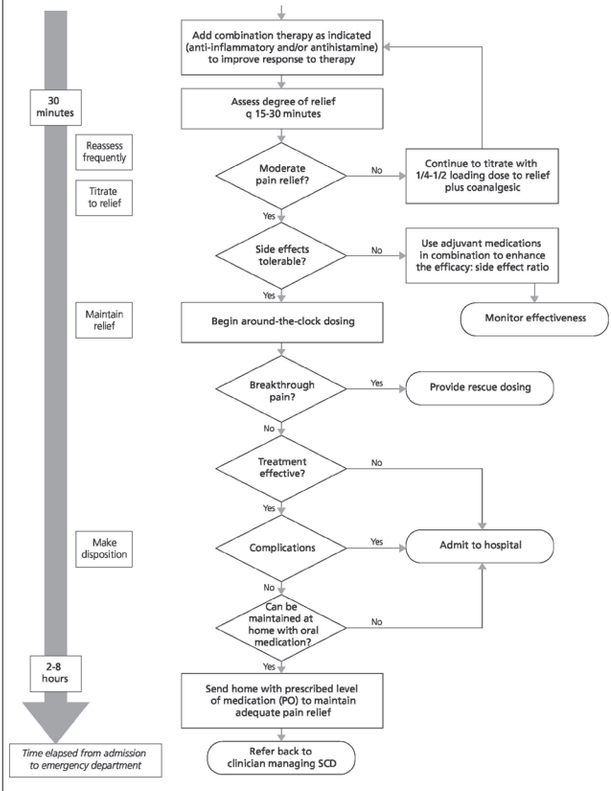
## ED Evaluation and Treatment (continued)

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