

Sickle Cell Acute Chest Syndrome

June 24, 2020 by [Josh Farkas](#)



(<https://emcrit.org/ibcc/sickle-chest/attachment/sicklestop/>)

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pathophysiology

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sickle cell anemia & sickle cell disease

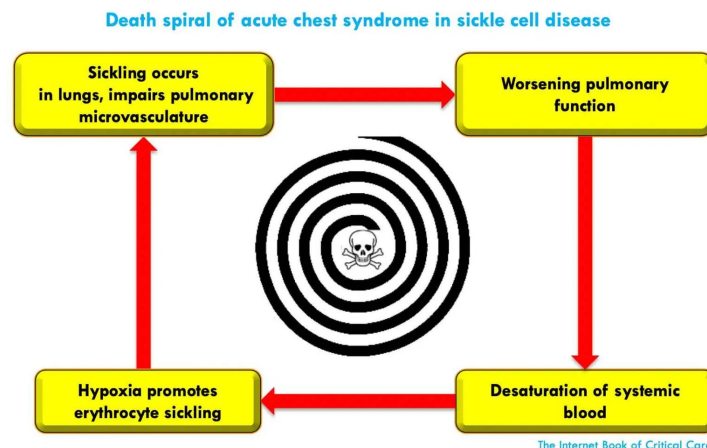
- *Sickle cell anemia* is an autosomal recessive genetic disorder causing a mutation in hemoglobin which causes it to polymerize, causing erythrocyte deformity (in a "sickle" configuration). Sickled erythrocytes are prone to hemolysis or occlusion of capillaries. The abnormal hemoglobin is termed "Hemoglobin S," whereas normal hemoglobin is termed Hemoglobin A.
- Some patients are *compound heterozygotes* who have one Hemoglobin S gene and also also another abnormal hemoglobin gene (e.g., Hemoglobin C or beta-thalassemia). These patients also experience erythrocyte sickling and are overall treated similarly to patients with sickle cell anemia. The term "sickle cell disease" is used as an umbrella term to refer to patients who experience erythrocyte sickling (whether due to genotype SS or various compound heterozygotes).

vaso-occlusive crises

- Patients with sickle cell disease occasionally experience episodes where erythrocytes sickle, leading to microvascular occlusion. Most frequently this affects bones, leading to extremity pain.
- Factors which may promote erythrocyte sickling (and vaso-occlusive crises) include:
 - *Hypoxemia* is the strongest stimulus for sickling (*deoxygenated* hemoglobin S is less soluble).
 - Acidosis
 - Dehydration
 - Infection and inflammation
 - Fever
 - Stasis of blood (e.g., reduced cardiac output)

acute chest syndrome

- This may be roughly conceptualized as a vaso-occlusive crisis which involves the lungs.
- Occlusion of microvasculature in the lungs is potentially life-threatening, because this can initiate a vortex of worsening hypoxemia (which in turn exacerbates sickling, as shown below).



<https://emcrit.org/ibcc/sickle-chest/attachment/sicklevortex/>

epidemiology

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general epidemiology

- Sickle cell disease is the most common genetic disease in the world. ([32445595](https://pubmed.ncbi.nlm.nih.gov/32445595/) (<https://pubmed.ncbi.nlm.nih.gov/32445595/>.)
- Acute chest syndrome occurs in the majority of people with sickle cell anemia at some point during their lives.

mortality

- Acute chest syndrome is responsible for roughly 25% of deaths among people with sickle cell disease.
 - The mortality of a single episode is estimated at ~3-9%. ([29648482](https://pubmed.ncbi.nlm.nih.gov/29648482/) (<https://pubmed.ncbi.nlm.nih.gov/29648482/>.) This is equivalent to the mortality rate of patients with STEMI. ([27099764](https://pubmed.ncbi.nlm.nih.gov/27099764/) (<https://pubmed.ncbi.nlm.nih.gov/27099764/>.)
-

trigger of acute chest syndrome

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infection (~25%)

- Atypical bacteria (e.g., chlamydia or mycoplasma species)
- Typical bacterial pathogens
- Viruses (respiratory syncytial virus, parvovirus B19, COVID-19)

noninfectious

- Painful vaso-occlusive crisis (*most common cause*, with acute chest syndrome often occurring 1-3 days after pain onset)
 - Surgical procedures (post-operative sickle chest syndrome)
 - Pulmonary embolism
 - Asthma
 - Pulmonary edema
 - Atelectasis of any etiology
 - Opioid causing hypoventilation
-

symptoms

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- Chest pain (~50-80%), may be pleuritic or bone pain.
 - Dyspnea (~50%)
 - Fever
 - Cough
 - Hemoptysis
 - May present with other features of vaso-occlusive crisis:
 - Neurological symptoms in ~20% of patients (may relate to fat emboli syndrome due to an underlying vaso-occlusive crisis). These may include delirium, seizure, and stroke.
 - Extremity pain
-

examination & POCUS

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hypoxia

- Hypoxemia may be an early finding (preceding other signs or X-ray abnormalities). ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/) (<https://pubmed.ncbi.nlm.nih.gov/25824256/>.)
- Hypoxia in a patient with sickle cell disease should always raise concern for possible acute chest syndrome.
- Some patients may have chronic hypoxemia (e.g., due to pulmonary hypertension), so changes from baseline oxygenation are relevant.

lung sonography

- Lung ultrasonography appears to be more sensitive than chest X-ray for acute chest syndrome. Among patients admitted with vaso-occlusive crisis who subsequently developed acute chest syndrome, abnormalities on lung ultrasonography were visible about a day earlier than abnormalities on chest x-ray. ([30017686](https://pubmed.ncbi.nlm.nih.gov/30017686/) (<https://pubmed.ncbi.nlm.nih.gov/30017686/>))
- Findings in acute chest syndrome include pulmonary consolidation, B-lines, and pleural effusions. ([26886600](https://pubmed.ncbi.nlm.nih.gov/26886600/) (<https://pubmed.ncbi.nlm.nih.gov/26886600/>)) These abnormalities certainly aren't specific for acute chest syndrome. Interpretation requires integration with the clinical context and prior chest imaging (e.g., archival CT scans if available).

cardiac sonography

- Sickle cell disease may cause chronic pulmonary hypertension with right ventricular dilation. Thus, right ventricular dilation isn't necessarily indicative of acute pulmonary embolism. Furthermore, McConnell's sign can occur in sickle cell disease without acute pulmonary embolism. ([29498079](https://pubmed.ncbi.nlm.nih.gov/29498079/) (<https://pubmed.ncbi.nlm.nih.gov/29498079/>))

radiology

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chest X-ray

- Infiltrates are often seen (and technically, based on the definition of acute chest syndrome, this is a diagnostic requisite).
- Pleural effusions are common.
- Radiologic findings may lag behind physical signs, so the chest X-ray may be normal early in the disease course. Likewise, even if chest X-ray abnormalities are present, they may under-estimate disease severity. ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/) (<https://pubmed.ncbi.nlm.nih.gov/25824256/>))

CT scan to evaluate for PE?

- Routine chest CT scan is unnecessary, but CT should be performed if there is concern for PE.
- Sickle cell anemia causes increased risk of PE for a variety of reasons (frequent hospitalization, hypercoagulable state, and impaired fibrinolysis). ([29648482](https://pubmed.ncbi.nlm.nih.gov/29648482/) (<https://pubmed.ncbi.nlm.nih.gov/29648482/>)) Patients with sickle cell disease usually have elevated D-dimer, so measurement of the D-dimer is generally unhelpful. ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/) (<https://pubmed.ncbi.nlm.nih.gov/25824256/>))
- Independent factors suggesting the presence of PE are listed below. If two or more of these are present, evaluation for PE may be considered. ([28905364](https://pubmed.ncbi.nlm.nih.gov/28905364/) (<https://pubmed.ncbi.nlm.nih.gov/28905364/>))
 - Lack of an evident trigger for acute chest syndrome.
 - Baseline hemoglobin >8.2 g/dL.
 - Platelet count >440 b/L.
 - PaCO₂ < 38mm (if measured).

laboratory studies

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general labs to obtain:

- Complete blood count
- Hemoglobin electrophoresis to determine % Hemoglobin S
- Blood for type & screen.
- Coagulation factors (INR, PTT, fibrinogen)
- Electrolytes, including calcium level (ionized calcium level if available)
- Liver function tests

investigation of cause

- Blood and sputum culture
- Procalcitonin
- Nasopharyngeal PCR to evaluate for relevant viral pathogens (e.g., COVID-19, influenza, respiratory syncytial virus)

rapid progression & multi-organ failure syndrome

[\(back to contents\) \(#top\)](#)**what is this?**

- Rapid progression is defined as a progression from developing pulmonary symptoms to requiring at least 3 liters of oxygen in <24 hours. This is often associated with multi-organ failure (including renal failure, delirium, and hepatic dysfunction).[\(27543812 \(https://pubmed.ncbi.nlm.nih.gov/27543812/\)\)](https://pubmed.ncbi.nlm.nih.gov/27543812/)
- Rapid progression often seems to be the result of systemic involvement from *fat emboli syndrome*, as a result of bone marrow necrosis.

clinical findings may include:

- Greater drop in hemoglobin from baseline.
- Absolute and relative thrombocytopenia (compared to the patient's baseline) are the strongest predictors of rapid progression.
- Acute kidney injury.
- Delirium.

TABLE II. Characteristics, treatment and outcomes of adults with Hemoglobin SS or Hemoglobin SB₀ thalassemia (referred to as sickle cell anemia (SCA)). During hospitalization for an index episode of acute chest syndrome (ACS) (N=76). Each individual only contributed one ACS, either the most severe or recent.

Variable	All adults, ≥20 years (N=76)	No Rapidly progressive ACS (N=60)	Rapidly progressive ACS (N=16)	P (univariate)
Age at index ACS (years), median (IQR)	27 (24, 31)	26 (24,32)	31 (25.5, 32.5)	0.762
Male sex, n (%)	48 (63.2)	37 (61.7)	11 (68.8)	0.602
Hemoglobin genotype				
HbSS, n (%)	65 (85.5)	54 (90.0)	11 (68.8)	0.019
HbS-beta-thalassemia, n (%)	11 (14.5)	6 (10.0)	5 (31.3)	
Hydroxyurea therapy, n (%)	50 (65.8)	40 (66.7)	10 (62.5)	0.755
Asthma, n (%)	16 (21.3)	11 (18.6)	5 (31.3)	0.275
Pulmonary hypertension, n (%)	13 (17.1)	8 (13.3)	5 (31.3)	0.091
Nephropathy, n (%)	7 (9.2)	3 (5.0)	4 (25)	0.014
Laboratory findings during ACS				
Baseline fetal hemoglobin (%), median (IQR)	7.70 (10.0)	7.50 (11.0)	8.30 (8.00)	0.972
Baseline Hemoglobin (g/dL) ^a , median (IQR)	8.90 (1.60)	8.70 (1.70)	9.15 (1.60)	0.172
Hemoglobin at presentation ^a , median (IQR)	7.10 (1.50)	7.45 (1.60)	6.70 (0.90)	0.006
Decrease in hemoglobin from baseline, median (IQR)	2.00 (2.10)	1.80 (1.60)	2.95 (1.16)	<0.001
Baseline platelet count (×10 ⁹ /L) ^a , median (IQR)	316.0 (147.0)	316.0 (150.0)	344.0 (139.0)	0.877
Lowest platelet count in first 24 hours (×10 ⁹ /L), median (IQR)	179.0 (190.0)	215.5 (247.0)	146.0 (96.0)	0.012
Decrease in platelet count from baseline (×10 ⁹ /L), median (IQR)	101.5 (180.7)	94.0 (154.75)	195.0 (171.5)	0.035
Peak serum creatinine (mg/dl), median (IQR)	0.84 (1.0)	0.80 (0.0)	2.14 (4.0)	<0.001
Maximal respiratory support during ACS				
<3 L oxygen, n (%)	55 (75.4)	51 (85.0)	0 (0.0)	<0.001
≥3 L oxygen, n (%)	8 (11)	7 (11.7)	5 (31.3)	
Intubation and mechanical ventilation, n (%)	13 (17.1)	2 (3.3)	11 (68.8)	
Complications and associated findings				
Worsening anemia (Hb decrease by >2 g/dl from baseline), n (%)	63 (82.9)	47 (78.3)	16 (100.0)	0.041
Thrombocytopenia (platelet count <150 × 10 ⁹ /L or 50% drop from baseline), n (%) ^b	38 (50)	25 (40.8)	13 (81.3)	0.005
Altered mental status, n (%)	14 (18.4)	7 (11.7)	7 (43.8)	0.003
Other neurologic complication including stroke and seizures, n (%)	14 (18.4)	9 (15.0)	5 (31.3)	0.136
Acute kidney injury, n (%)	13 (17.1)	2 (3.3)	11 (68.8)	<0.001
Liver function impairment, n (%)	21 (27.6)	9 (15.0)	12 (75.0)	<0.001
Total duration of hospitalization (days), median (IQR)	8 (5,14)	7 (5,10)	14 (7,23)	0.027

ACS indicates acute chest syndrome, IQR indicates interquartile range.

^a Baseline laboratory studies refer to the mean of values obtained at outpatient visits at times when the patient was in their baseline state of health and not acutely ill.

^b 39.2% patients had absolute thrombocytopenia defined as a platelet count <150 × 10⁹/L.

Chaturvedi S et al. 2016 PMID 27543812

<https://emcrit.org/ibcc/sickle-chest/attachment/chatrapid/>

definition & differential considerations

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definition of acute chest syndrome

- Acute chest syndrome is a clinical *syndrome* which is defined as the combination of:
 - (1) A new opacity on chest x-ray.
 - (2) Fever and/or respiratory symptoms (e.g., cough, dyspnea, or chest pain).
- This is an *intentionally broad* definition which doesn't exclude other diagnoses. For example, it's common for a patient to have *both* sickle cell acute chest syndrome *and* bacterial pneumonia. In this situation, *both* conditions should be vigorously treated.

differential diagnoses to consider include:

- Myocardial infarction.
- Decompensated chronic cor pulmonale.
- Pulmonary embolism.
- Splenic sequestration crisis (can occur along with a chest crisis; suggested by a rapid drop in hemoglobin).
- Overwhelming post-splenectomy sepsis (patients with sickle cell disease may eventually develop splenic infarction and become functionally asplenic).
- Line infection (among patients with chronic indwelling lines or ports).

aggressive oxygenation & monitoring

target

- Establishing adequate oxygenation is essential to prevent progressive sickling of erythrocytes.
- No specific evidence-based target exists.
- A commonly recommended target is an oxygen saturation of >92%. ([29648482 \(https://pubmed.ncbi.nlm.nih.gov/29648482/\)](https://pubmed.ncbi.nlm.nih.gov/29648482/)) However, British guidelines recommend targeting a saturation >95% or within 3% of the patient's baseline (among patients with chronic hypoxemia). ([25824256 \(https://pubmed.ncbi.nlm.nih.gov/25824256/\)](https://pubmed.ncbi.nlm.nih.gov/25824256/))

respiratory support

- High-flow nasal cannula (HFNC) or BiPAP may be used, depending on the clinical scenario.
- Avoiding atelectasis is essential (e.g., using an incentive spirometer, early ambulation, or BiPAP).
 - **Incentive spirometry** has been shown to prevent chest syndrome among patients admitted with painful vaso-occlusive crises. ([7637747 \(https://pubmed.ncbi.nlm.nih.gov/7637747/\)](https://pubmed.ncbi.nlm.nih.gov/7637747/)) This should be considered for acute chest syndrome, depending on the clinical context (e.g., if the patient is strong enough to comply with it).
 - BiPAP may be a more effective strategy to avoid atelectasis in the context of acute illness.
- If adequate oxygenation can't be promptly achieved with noninvasive support, then intubation should be pursued.


bronchodilators


- Bronchodilators aren't generally indicated in acute chest syndrome.
- These should be considered for patients with asthma, COPD, or clinical evidence of bronchospasm.

disposition

- Clinical deterioration can occur rapidly and unexpectedly. ([29648482](https://pubmed.ncbi.nlm.nih.gov/29648482/))
- Careful monitoring is necessary to facilitate early detection and intervention for desaturation.
- ICU admission should be considered for patients requiring substantial oxygen support.

general considerations regarding transfusion

 Send a type & crossmatch blood sample *early* (it may take a while).

 Communicate early & often with the blood bank.

risks/benefits?

- Benefit: Helps prevent ongoing erythrocyte sickling. Exchange transfusion may largely eliminate sickle hemoglobin, thereby temporarily "curing" the disease.
- Risks: Transfusion always carries several risks, but these are overall relatively low. Patients with sickle cell disease are at increased risk of transfusion reaction, given their history of numerous transfusions.
- There is no high-level evidence to support transfusion. However, this is physiologically rational and widely believed to be a cornerstone of the management of severe acute chest syndrome.

additional considerations surrounding transfusion in sickle cell disease

- Make sure the blood bank is aware that the patient has sickle cell anemia. They should be able to ensure proper matching and take precautions to avoid transfusion reactions. This involves several components:
- (#1) Preventative matching of antigens E, C, and Kell may avoid alloimmunization (often a problem in sickle cell disease).
 - Matching of antigens E, C, and Kell is not typically done in patients who don't have sickle cell disease. However, among patients with sickle cell disease, *preventative* matching of these antigens may help avoid alloimmunization. Some blood banks may match additional antigens as well.
- (#2) Using leukoreduced blood reduces the incidence of febrile transfusion reactions and avoids alloimmunization against HLA antigens (which can be problematic for patients requiring stem cell or organ transplantation later on).

- (#3) If possible, transfusion from a blood donor with sickle cell trait should be avoided.

hyperhemolysis syndrome ([30198607](https://pubmed.ncbi.nlm.nih.gov/30198607/))

- A life-threatening hemolytic transfusion reaction can occur in sickle cell disease, with destruction of *both* the patient's erythrocytes and the transfused erythrocytes.
- Diagnosis: Post-transfusion hemoglobin is *lower* than pre-transfusion hemoglobin. Labs show elevated lactate dehydrogenase, hemoglobinuria, and hyperbilirubinemia. Patients may have pain and fever.
- Management:
 - Avoid additional red cell transfusion if possible (further transfusion may aggravate hemolysis).
 - Consult with hematology, consider steroid and intravenous immunoglobulin (IVIG).

simple transfusion aka top-up transfusion

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This simply involves administration of packed red blood cells. Simple transfusion *should be considered early*, as this is often effective at preventing disease progression. ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/))

indications for a simple transfusion

- (1) Patient is mildly anemic (e.g., HgB <7 mg/dL) *and* not severely ill.
- (2) Patient is severely anemic (e.g., HgB <5 mg/dL) *and* is severely ill. In this situation, given the pre-existing anemia, it may be possible to achieve a fairly low fraction of sickle hemoglobin (<50%) simply by transfusing the patient up to a hemoglobin of ~10 mg/dL.
 - Very ill patients may require an exchange transfusion *following* simple transfusion, to further reduce the percent hemoglobin S.

optimal post-transfusion hemoglobin target?

- 10-11 mg/dL seems to be a general consensus in the literature (in the absence of any robust evidence). ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/))
- Transfusion to >11 mg/dL could potentially increase blood viscosity, which may cause clinical *hyperviscosity syndrome* (impaired brain perfusion due to the combination of a high total hemoglobin plus a high fraction of sickle hemoglobin).
- If simple transfusion inadvertently results in a post-transfusion hemoglobin >12 mg/dL, then therapeutic phlebotomy is advisable to reduce blood viscosity.

exchange transfusion

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Exchange transfusion is more powerful than simple transfusion, because this allows for a rapid and dramatic reduction in the sickle hemoglobin (*without* increasing the blood viscosity).

indications

- There are no clear-cut indications for exactly when to perform exchange transfusion. This should be considered for patients with more severe disease, for example:
 - "Severe hypoxemia" (Guidelines recommend this as an indication for exchange transfusion, without clearly defining it. Perhaps this might refer to patients requiring >2-4 liters nasal cannula?). ([31985807](https://pubmed.ncbi.nlm.nih.gov/31985807/))
 - Rapidly progressive lung involvement (e.g., deterioration over hours rather than days).
 - Evolving multi-organ failure (e.g., respiratory failure *plus* confusion or acute renal failure).
 - Failure to improve despite simple transfusion.
 - High risk of adverse outcomes (e.g., pregnant women or patients with numerous comorbidities).
- Given the lack of solid evidence, consultation with hematology should be sought if it's unclear whether exchange transfusion is needed.

contraindications


- Exchange transfusion isn't advisable for patients with severe anemia (e.g., hemoglobin <6 mg/dL).

- Such patients should *first* undergo simple transfusion (see [above \(#simple_transfusion\)](#)).
- Following simple transfusion, an exchange transfusion may be considered (if still indicated).
- Severe hypocalcemia could be worsened by administration of blood products containing citrate buffer.

therapeutic targets

- There is no high-quality data, but the following are consensus targets.
- (1) % Hemoglobin S is usually decreased to target <30%.
 - However, in the sickest patients (e.g., intubated patients), targeting <20% hemoglobin S may be considered. ([25824256](https://pubmed.ncbi.nlm.nih.gov/25824256/) (<https://pubmed.ncbi.nlm.nih.gov/25824256/>)) ([30910617](https://pubmed.ncbi.nlm.nih.gov/30910617/) (<https://pubmed.ncbi.nlm.nih.gov/30910617/>))
- (2) Total hemoglobin concentration is usually targeted to ~10 mg/dL. ([30910617](https://pubmed.ncbi.nlm.nih.gov/30910617/) (<https://pubmed.ncbi.nlm.nih.gov/30910617/>))

estimating the number of units to exchange transfuse

- A typical adult may require ~5-8 units of red blood cells during an exchange transfusion. However, this may vary depending on several factors.
- Ideally, the percent hemoglobin S may be measured directly and used to determine how many units of blood will be required. If the percent hemoglobin S cannot be measured rapidly, then it can be estimated to be 100% (assuming that the patient has sickle cell anemia and hasn't undergone transfusion recently).
-  [This MDCalc formula](https://www.mdcalc.com/sickle-cell-rbc-exchange-volume) (<https://www.mdcalc.com/sickle-cell-rbc-exchange-volume>) may be used to more precisely estimate the number of units required. The following estimates may be needed:
 - If the percent sickle hemoglobin isn't known, it may be estimated at 100%.
 - The goal HgbS is generally 30%.
 - The hematocrit of transfused RBCs is generally ~57%. ([30198607](https://pubmed.ncbi.nlm.nih.gov/30198607/) (<https://pubmed.ncbi.nlm.nih.gov/30198607/>))

techniques for exchange transfusion

- (1) Standard technique is to use an erythrocytapheresis machine, which continuously removes the patient's blood, centrifuges it, and exchanges erythrocytes (similarly to leukapheresis). This procedure will be supervised and performed by the blood bank and hematology.
- (2) If erythrocytapheresis isn't logistically feasible, manual exchange transfusion may be needed (the technique for this is below).


vascular access

- Some patients may have an AV fistula or a chronic port, which might be an option.
- For emergent exchange transfusion, large bore central access is ideal. Preferred options might include:
 - i) [Trialysis catheter](https://bardaccess.com/products/dialysis/power-trialysis/) (<https://bardaccess.com/products/dialysis/power-trialysis/>) (hemodialysis catheter with an additional port, for a total of three lumens).
 - ii) Standard, two-lumen hemodialysis catheter.
 - iii) [Multi-Access Catheter \(MAC\)](https://www.teleflex.com/la/en/product-areas/vascular-access/multi-access-catheter/index.html) (<https://www.teleflex.com/la/en/product-areas/vascular-access/multi-access-catheter/index.html>) or similar device (a multi-lumen access device which includes a large-bore central access port).

manual exchange transfusion

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indications

-  Generally erythrocytapheresis is preferred over manual exchange transfusion. Manual exchange transfusion may be considered if erythrocytapheresis is unavailable.
- Manual exchange will cause loss of plasma and platelets in addition to erythrocytes. This may be good or bad, depending on the context:
 - Loss of platelets could be dangerous in the context of hemorrhage or thrombocytopenia.
 - Some authors argue that removal of plasma is beneficial, which could make manual exchange a superior procedure. ([28470719](https://pubmed.ncbi.nlm.nih.gov/28470719/) (<https://pubmed.ncbi.nlm.nih.gov/28470719/>))

general technique for manual exchange transfusion ([28584527](https://pubmed.ncbi.nlm.nih.gov/28584527/) (<https://pubmed.ncbi.nlm.nih.gov/28584527/>))

- **[Step #1]** Two-unit exchange:

- **#1A)** Bleed the patient, by a volume that varies depending on baseline hemoglobin as shown below. Withdrawal of blood may be achieved using gravity to an empty bag, or a 50-ml syringe with a 3-way stopcock.
 - If baseline hemoglobin is 6-8 g/dL → bleed 250 ml.
 - If baseline hemoglobin is 8-10 g/dL → bleed 500 ml.
 - If baseline hemoglobin is 10-12 g/dL → bleed 750 ml total (in two divided phlebotomies; see #1B).
 - If baseline hemoglobin is >12 g/dL → bleed 1,000 ml total (in two divided phlebotomies; see #1B).
- **#1B)** Infuse a volume of crystalloid equal to the volume of blood removed in #1A.
 - For patients being phlebotomized 750-1000 ml, this may be performed in two stages to prevent hypovolemia (First remove 375 or 500 ml blood, replace with 375 or 500 ml crystalloid, then remove an additional 375 or 500 ml blood and replace again with crystalloid).
 - If there is sufficient vascular access, both bleeding and crystalloid infusion may be performed *simultaneously* (steps #1A & #1B) ([30713307 \(https://pubmed.ncbi.nlm.nih.gov/30713307/\)](https://pubmed.ncbi.nlm.nih.gov/30713307/))
- **#1C)** Infuse two units of packed red blood cells.
- **#1D)** Infuse crystalloid in equal volume to the amount of packed cells administered (this will be roughly ~500 ml).
- **[Step #2]** Re-assess:
 - Complete blood count (target a hemoglobin level of ~10 mg/dL).
 - Electrolytes, including calcium (note that citrate and crystalloid may affect acid/base status and calcium level)([28362411 \(https://pubmed.ncbi.nlm.nih.gov/28362411/\)](https://pubmed.ncbi.nlm.nih.gov/28362411/))
 - May consider measuring % hemoglobin S if this can be rapidly measured (in most hospitals it can't be measured promptly, so don't delay treatment while waiting for it).
- **[Step #3]** If the post-exchange hemoglobin is >12 mg/dL, remove 500 ml blood to avoid hyperviscosity.
- **[Step #4]** Perform repeated exchanges (steps #1-3) as needed to achieve the target number of exchanged units (e.g., 4-8 units total).

modifications to this procedure depending on patient specifics

- For patients with active bleeding or high risk of bleeding, replacement of plasma with fresh frozen plasma (FFP) could be considered (along with closer monitoring of coagulation factors and fibrinogen).
- Whether to use 5% albumin or crystalloid as a replacement fluid isn't well defined. For most patients this probably doesn't matter.
- The choice of crystalloid could be varied depending on the patient's electrolytes and especially on acid-base status (more on this [here \(https://emcrit.org/ibcc/fluid/\)](https://emcrit.org/ibcc/fluid/)).

manual whole blood exchange

- Manual whole blood exchange involves removal of the patient's blood and replacement with whole blood. Since whole blood contains a balance of erythrocytes and plasma, no additional crystalloid is necessary.
- Whole blood exchange could theoretically be attractive if available. ([28470719 \(https://pubmed.ncbi.nlm.nih.gov/28470719/\)](https://pubmed.ncbi.nlm.nih.gov/28470719/)) However, most blood banks do not offer whole blood exchange.

volume resuscitation

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underlying concepts

- Hypovolemia could increase blood viscosity and thereby increase sickling. Thus, the use of maintenance fluid infusions has been widely recommended. However, maintenance fluid in critically ill patients is usually not recommended overall, as this may lead to volume overload over time (especially in patients with acute lung injury or cardiac dysfunction).
- There is no high-quality evidence on fluid administration in acute chest syndrome. ([25764071](https://pubmed.ncbi.nlm.nih.gov/25764071/))
- Sickle cell anemia causes renal difficulties in generating concentrated urine, which may lead to excessive water losses via the kidney.
- Sickle cell disease may cause *heart failure* and subsequent fluid retention, even in young adults (who would generally not be expected to have heart failure).

conclusions on fluid administration?

- Fluid administration should be personalized on the basis of history (e.g., adequacy of oral intake) and physical examination (e.g., bedside echocardiography).

- There is no evidence that *hypervolemia* improves sickle cell disease. Thus, the goal should be to establish and maintain a state of *euvolemia*.
- Follow fluid inputs and outputs.
- Follow daily electrolytes. If hypernatremia develops, this reveals a free water deficiency which must be [aggressively managed](https://emcrit.org/ibcc/hypernatremia/#treatment_free_water_replacement) (https://emcrit.org/ibcc/hypernatremia/#treatment_free_water_replacement).
- Most patients probably don't warrant continuous infusions of "maintenance" fluid (especially if they are receiving adequate nutrition).

antibiotics

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- Clinically it's often impossible to differentiate acute chest syndrome from pneumonia (the two disorders frequently co-exist).
- If there any concerns about possible pneumonia, patients should be empirically treated for this (e.g., by using a combination of azithromycin plus ceftriaxone). Over time, antibiotics may be modified based on culture and procalcitonin results.

pain management

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scope of the problem

- Patients may have pain for a variety of reasons. For example, vaso-occlusive crises may cause limb or rib pain.
- Inadequate control of chest pain may lead to splinting with consequent atelectasis, exacerbating hypoxemia.
- Patients often have a history of opioid treatment, rendering them less sensitive to opioids.
- Some patients may have altered mental status (e.g., due to fat embolization), increasing the risk of delirium or of respiratory suppression due to opioid. Furthermore, opioid may suppress the cough reflex and thereby promote atelectasis and hypoventilation. ([29648482](https://pubmed.ncbi.nlm.nih.gov/29648482/) (<https://pubmed.ncbi.nlm.nih.gov/29648482/>))
- NSAIDs should often be avoided, given the propensity of patients with severe acute chest syndrome to develop renal failure.

approach

- The overall approach is similar to that for any critically ill patient with pain. However, increased attention is required in this context, because it will be harder to strike the right balance.
- A pain-dose ketamine infusion may be extremely useful as an adjunctive analgesic agent which will not suppress respiration. This is especially useful in patients who may be less responsive to opioids. ([29791238](https://pubmed.ncbi.nlm.nih.gov/29791238/) (<https://pubmed.ncbi.nlm.nih.gov/29791238/>))
- A multi-modal approach is often most successful, for example:
 - (1) Scheduled oral acetaminophen 1 gram q6hrs.
 - (2) Ketamine infusion 0.1-0.3 mg/kg/hour.
 - (3) Opioid use as needed, with precise titration (e.g., consider Patient Controlled Analgesia).
 - (4) A lidocaine patch may be helpful for localized pain.
 - (5) Intercostal nerve blocks may provide 18-24 hours of pain relief without other associated risks. ([29648482](https://pubmed.ncbi.nlm.nih.gov/29648482/) (<https://pubmed.ncbi.nlm.nih.gov/29648482/>))

acute chest syndrome in COVID-19 patients

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general concepts


- Sickle cell disease affects [100,000 people](https://www.cdc.gov/ncbddd/sicklecell/data.html) (<https://www.cdc.gov/ncbddd/sicklecell/data.html>) in the United States (~1/360 African Americans) and ~15,000 people in the United Kingdom. It is also common throughout the world, especially in India, Brazil, and Africa. This may be one factor contributing to the high mortality of COVID-19 in these patients.
- COVID-19 is notorious for causing hypoxemia. Although this may be tolerated by many patients, hypoxemia often *won't* be tolerated by patients with sickle cell disease. In this context, desaturation may cause widespread sickling of erythrocytes and acute chest syndrome.
- By definition, patients with sickle cell disease and COVID-19 pneumonia will meet the diagnostic criteria of acute chest syndrome.

- Older patients with long-standing sickle cell disease may have chronic pulmonary hypertension, which will further reduce their physiological reserve.
- Sickle cell disease may cause elevated lactate dehydrogenase and ferritin, which could confuse prognostic scoring systems used with COVID-19.

existing evidence regarding COVID-19 & sickle cell disease

- Evidence regarding COVID-19 in sickle cell disease is currently emerging and in an infantile state. Currently this consists of ~20 reported patients in individual reports and case series, which may tend to over-represent tertiary centers and patients who have recovered. ([32527955](https://pubmed.ncbi.nlm.nih.gov/32527955/) (<https://pubmed.ncbi.nlm.nih.gov/32527955/>), [32445595](https://pubmed.ncbi.nlm.nih.gov/32445595/) (<https://pubmed.ncbi.nlm.nih.gov/32445595/>), [32369606](https://pubmed.ncbi.nlm.nih.gov/32369606/) (<https://pubmed.ncbi.nlm.nih.gov/32369606/>), [32267016](https://pubmed.ncbi.nlm.nih.gov/32267016/) (<https://pubmed.ncbi.nlm.nih.gov/32267016/>), [32243621](https://pubmed.ncbi.nlm.nih.gov/32243621/) (<https://pubmed.ncbi.nlm.nih.gov/32243621/>), [32314798](https://pubmed.ncbi.nlm.nih.gov/32314798/) (<https://pubmed.ncbi.nlm.nih.gov/32314798/>))
- One of the twenty patients died, but the vast majority did well. This may reflect that most patients were relatively young (<40 YO). Transfusion support including red cell exchange was often utilized.
- Patients often present initially with pain due to a vaso-occlusive crisis. Acute chest syndrome may develop some days later. ([32369606](https://pubmed.ncbi.nlm.nih.gov/32369606/) (<https://pubmed.ncbi.nlm.nih.gov/32369606/>))

individual patient management

- Overall this consists of a *combination* of the treatment of COVID-19 *plus* the treatment of acute chest syndrome. The most important aspect is to remember both components (rather than overlooking the acute chest syndrome).
- Early simple transfusion up to a hemoglobin of ~10 mg/dL should be considered for patients with mild hypoxemia. This is relatively easy to accomplish and could deter further deterioration.
- *Early* exchange transfusion should be strongly considered for patients with worsening oxygenation, for the following reasons:
 - i) Exchange transfusion takes time to perform.
 - ii) Both COVID-19 and acute chest syndrome are prone to rapid deterioration. The superposition of these two pathologies may create a very unstable situation, where patients could deteriorate rapidly (before exchange transfusion could be accomplished).
- Due to logistic constraints imposed by the epidemic, it may be difficult to rapidly transfer patients to tertiary hospitals. Thus, *manual exchange transfusion* may need to be performed at hospitals which don't generally perform this. A description of this procedure is above.
- Both COVID-19 and sickle cell disease cause pro-thrombotic states, so the superimposition of these conditions may be very thrombogenic. Thus, there should be a high index of suspicion and vigorous evaluation for venous thromboembolic disease. More aggressive DVT prophylaxis may be warranted in this population; for example, one center used 1.5 mg/kg enoxaparin daily). ([32369606](https://pubmed.ncbi.nlm.nih.gov/32369606/) (<https://pubmed.ncbi.nlm.nih.gov/32369606/>)) Another option with a considerable evidentiary basis overall is [enoxaparin 0.5 mg/kg q12hr](https://emcrit.org/pulmcrit/40-enoxaparin/) (<https://emcrit.org/pulmcrit/40-enoxaparin/>).
-  Whenever a sickle cell disease patient is admitted with COVID-19:
 - Notify the ICU and hematology teams. For hypoxemic patients, consider admission to ICU.
 - Talk to the blood bank about typing & crossmatching enough blood to perform an exchange transfusion if needed (e.g., ~6 units of packed cells).

blood supply management

- COVID-19 is a major threat to the blood supply, especially in regions where sickle cell disease is prevalent:
 - (1) Patients with COVID-19 and sickle cell disease may require frequent transfusion.
 - (2) Healthy blood donors may be afraid to venture into clinics to donate blood.
- Approaches to this problem may include:
 - Encouragement to donate blood. Sickle cell disease patients with antibodies to several blood antigens may be most likely to cross-match with blood from African-American donors, so donation from these communities may be especially valuable.
 - In dire situations, *fresh whole blood transfusion* could be considered from a healthy donor with a matched blood type and minor antigens and who has been screened for infectious diseases. This involves phlebotomizing the donor and immediately infusing blood into the recipient, a technique utilized by some armies. ([26100776](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467507/) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467507/>))

prevention of acute chest syndrome

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- In some situations, a patient with sickle cell disease may be at extremely high risk of an impending acute chest crisis (e.g., a patient with an impending high-risk delivery or major surgical procedure).
- Prevention of acute chest syndrome may include:
 - Attention to maintaining excellent oxygenation.
 - Attention to maintaining euvolemia.
 - Avoidance of atelectasis.
 - Prophylactic transfusion may be considered (either simple transfusion or exchange transfusion). Hematology consultation may assist in assessing risks vs. benefits of transfusion support. ([30198607](https://pubmed.ncbi.nlm.nih.gov/30198607/) (<https://pubmed.ncbi.nlm.nih.gov/30198607/>))

summary

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Overview of sickle cell acute chest syndrome

imaging studies

- Chest X-ray
- POCUS (including lung & cardiac ultrasound)
- CT angiography to evaluate for PE if clinical suspicion

labs

- Investigation of trigger** (if necessary & context-dependent)
- Blood and sputum culture, possibly procalcitonin
 - Nasopharyngeal PCR for viral infection (e.g. COVID, flu, RSV)
 - Other tests as clinically indicated (e.g. urine legionella, pneumococcus antigens)

General labs to guide management

- Complete Blood Count (CBC)
- % Hemoglobin S based on electrophoresis (if possible)
- Type & screen (communicate early with blood bank)
- Coagulation factors (INR, PTT, fibrinogen)
- Electrolytes including calcium (ideally ionized Ca)
- Liver function tests

management generally involves:

- Aggressive respiratory support (raise sat >92%).
- Avoid atelectasis (e.g. BiPAP or incentive spirometry).
- Volume resuscitate to euvolemia.
- Antibiotics for PNA (including atypical coverage)
- Pain management (yet avoid respiratory suppression).
- Bronchodilators if asthma, COPD, or clinical bronchospasm.
- Consider simple or exchange transfusion (box below).

Possible indications for exchange transfusion

- Severe hypoxemia (e.g. >4-6 liters cannula)
 - Rapid deterioration (over hours)
 - Multi-organ involvement (e.g. AKI or delirium)
 - Failure to improve
 - High-risk patient (e.g. pregnant or comorbidity)
- These aren't absolute because there is no high-quality evidence here. Consult hematology early if doubt exists about whether transfusion is indicated.*

The Internet Book of Critical Care

[\(https://emcrit.org/ibcc/sickle-chest/attachment/sickleoverview/\)](https://emcrit.org/ibcc/sickle-chest/attachment/sickleoverview/)

podcast

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<https://i1.wp.com/emcrit.org/wp-content/uploads/2016/11/apps.40518.14127333176902609.7be7b901-15fe-4c27-863c-7c0dbfc26c5c.5c278f58-912b-4af9-88f8-a65fff2da477.jpg>



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questions & discussion

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To keep this page small and fast, questions & discussion about this post can be found on another page [here](https://emcrit.org/emcrit/sickle-chest/).



<https://i0.wp.com/emcrit.org/wp-content/uploads/2016/11/pitfalls2.gif>

- Patients with sickle cell anemia may be difficult to type and cross-match. Don't *wait* to type and screen the patient's blood until the patient needs a transfusion – send a type and screen *early*.
- Any patient with sickle cell disease who is desaturating should be considered to have acute chest syndrome until proven otherwise.
- Deterioration can occur rapidly and abruptly. Thus, close monitoring and a pro-active approach may be helpful.
- Acute chest syndrome can occur some days into an admission for painful extremity vaso-occlusive crisis. Thus, worsening oxygenation in a patient with sickle cell anemia should always raise concern for acute chest syndrome.

Going further

- [Best Case Ever – Acute Chest Syndrome](https://emergencymedicinecases.com/sickle-cell-acute-chest-syndrome/) (Anton Helman, Emergency Medicine Cases)
 - *This is an incredibly important case description which is highly recommended, only six minutes.*
- Radiopaedia, [Sickle Cell Acute Chest Syndrome](https://radiopaedia.org/articles/sickle-cell-disease-acute-chest-syndrome-1?lang=us), Dr Bahman Rasuli and Dr Yuranga Weerakkody et al.



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