



PACU

PHARMACY & ACUTE CARE UNIVERSITY

Acute Chest Syndrome Management in Sickle Cell Patients

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Objectives

- **Recognize** the epidemiology and pathophysiology of Acute Chest Syndrome (ACS) in sickle cell patients (Knowledge).
- **Interpret** early presentation and diagnostic criteria of ACS (Comprehension).
- **Apply** evidence-based treatment strategies for managing ACS in the emergency department

Case

- LS is a 42-year-old AA female who has a PMH of Sickle cell anemia (HbSS) and MDD. She presents to the ED with generalized pain in both her legs after failing her home pain medication regimen. The ED team commenced with VOC management and the patient was eventually admitted to the floor.
- On day 4 of admission LS develops fever, cough, chest pain, and respiratory distress. When a chest x-ray (CXR) was done it was revealed that the patient had pulmonary infiltrates and after ruling out other pathologies was diagnosed with ACS.



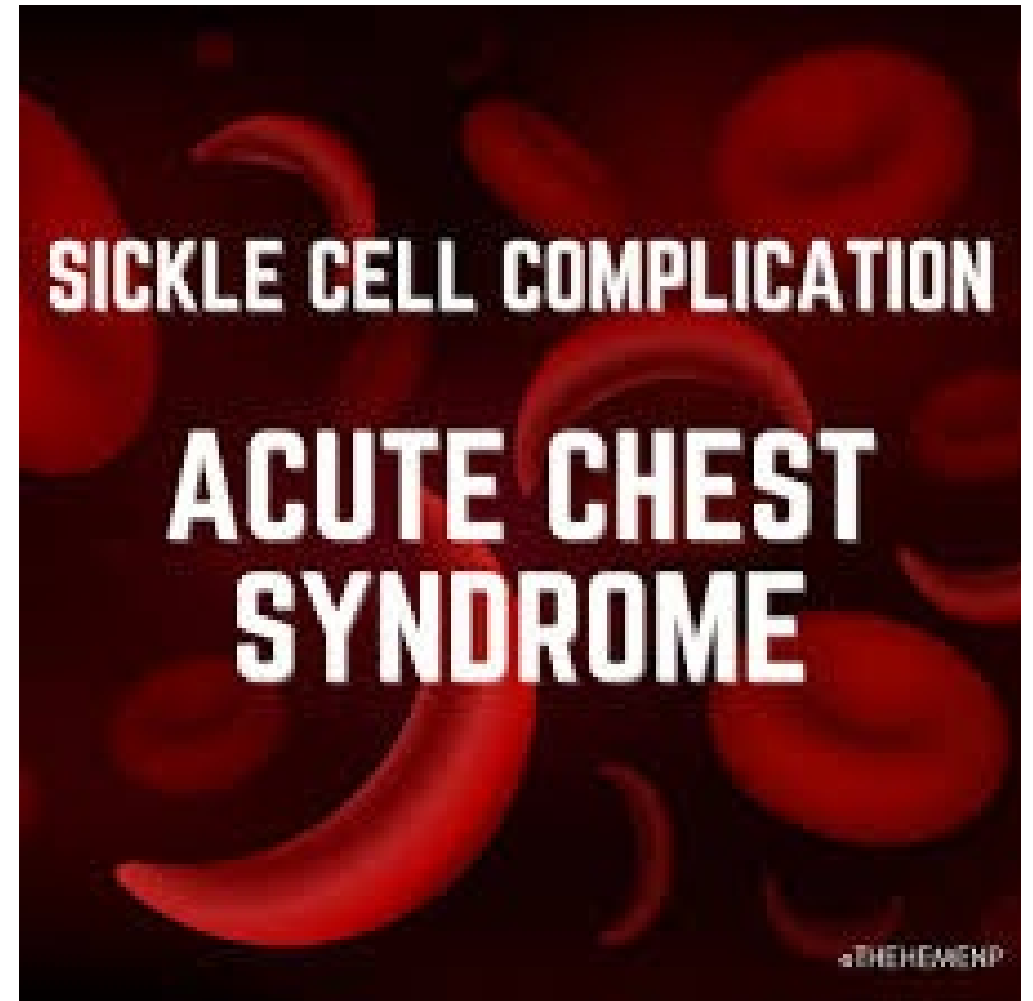
Case cont.

- Medications (Outpatient)
 - Opioids
 - Percocet 5/325mg 1-2 tablets every 4-6 hours as needed for pain
 - MS Contin 30mg BID
 - Non-Opioids
 - Sertraline 50mg daily
 - MVI daily
- Social/Family History
 - Lives with husband and 1 child
 - (-) smoking
 - (-) illicit substances
 - (+) alcohol occasionally (1-2 glass of wine ever couple months)
- Surgical History
 - C-Section (2018)
 - Bilateral total hip replacement (2021)



Overview of ACS

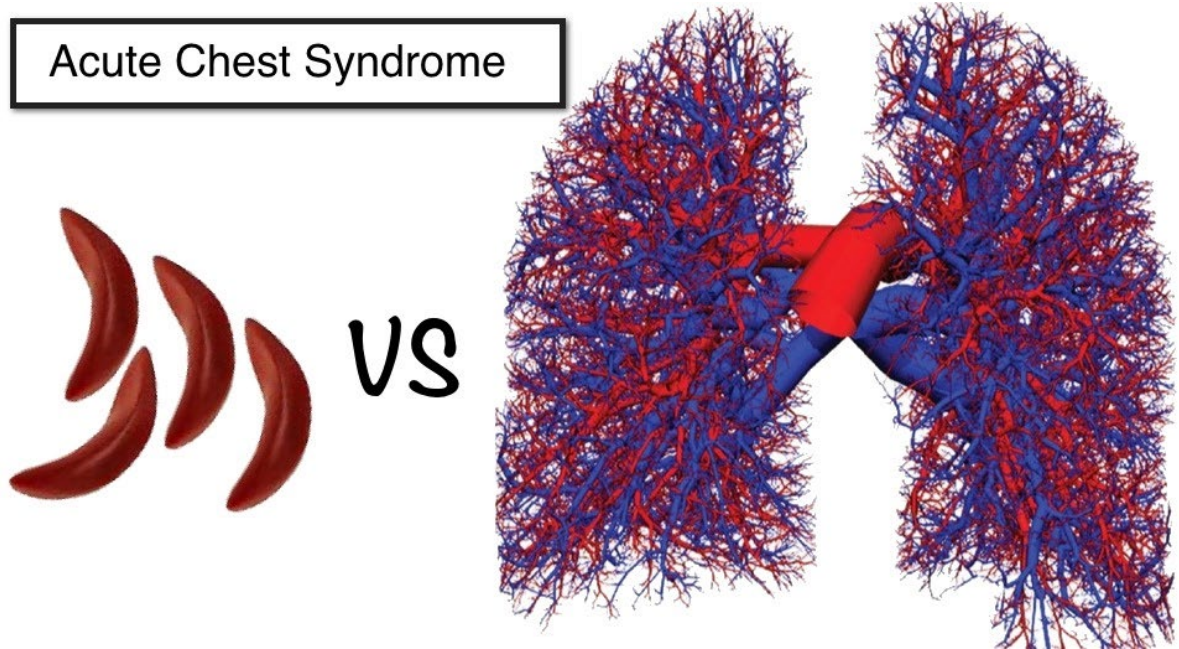
- ACS is a form of acute lung injury that involves vaso-occlusion within the pulmonary vasculature.
- ACS is a life-threatening thoracic complication that can result in lung injury, difficulty breathing, and low oxygen to the rest of the body.
- Important to note that ACS is considered a medical emergency and needs to be properly treated accordingly.





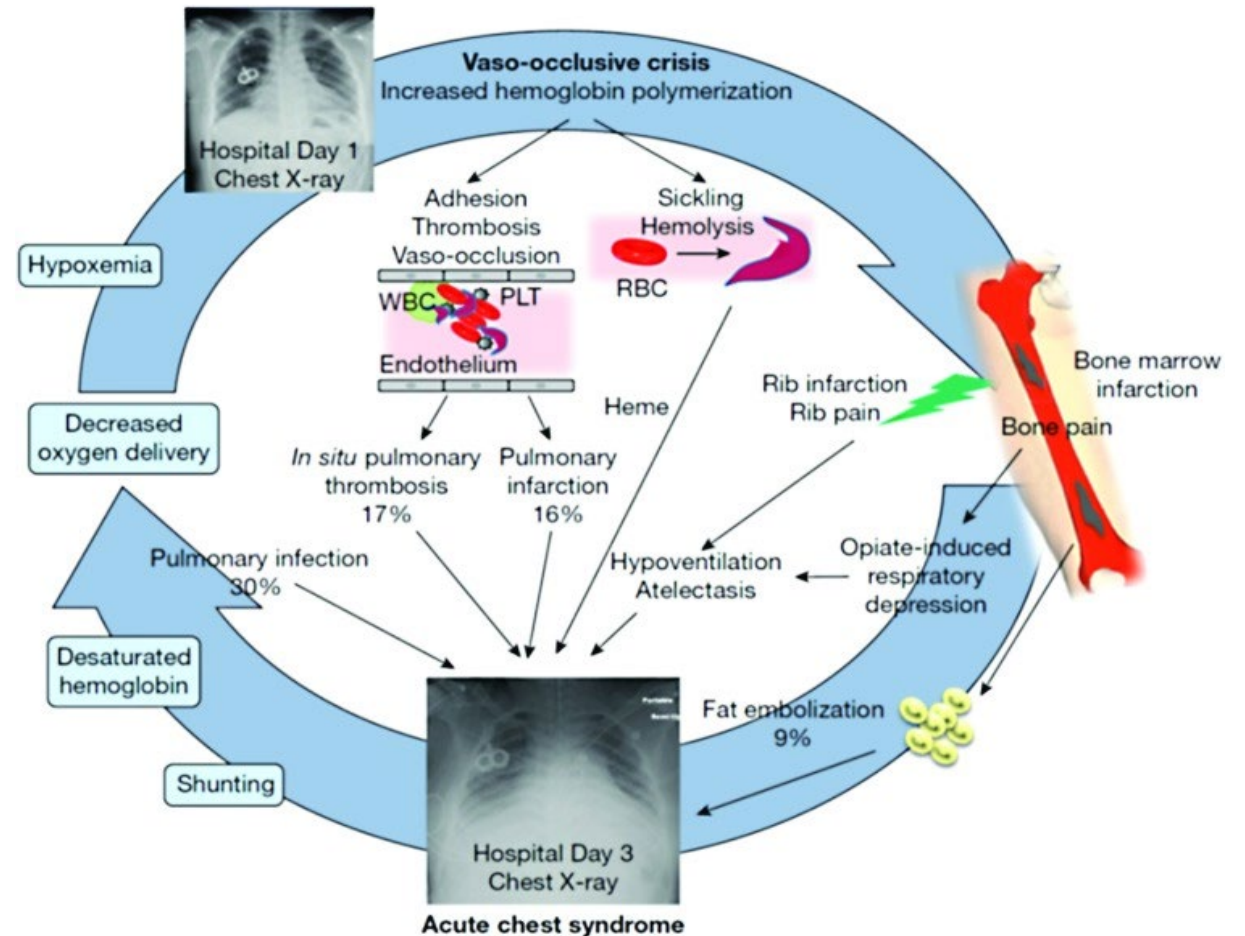
Overview of ACS cont.

- Vaso-occlusion pain is considered the leading cause of hospitalizations in patients with SCD. 10-20% of these patients develop ACS within 3 days of admission.
- ACS is considered the 2nd most common cause of hospitalization for SCD patients
- ACS accounts for approximately 25% of deaths in patients with SCD
- Its important to note that 80% of patients with ACS experience a VOC even prior to the episode of ACS



Pathophysiology of ACS

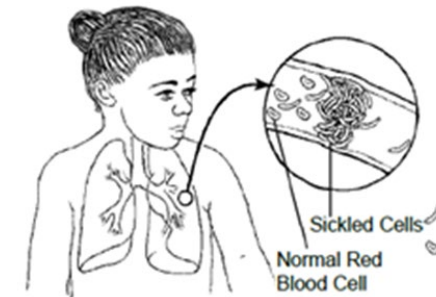
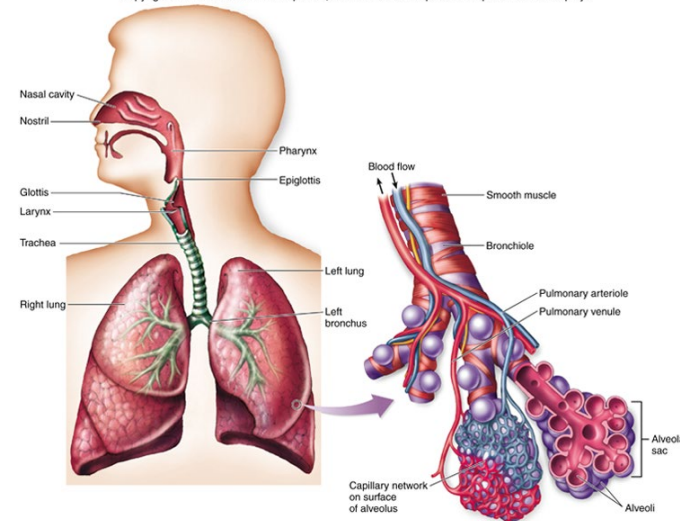
- The development of ACS represents a cycle of lung infarction, inflammation, and atelectasis leading to ventilation–perfusion mismatch and hypoxemia.
- Due to the nature of this disease state (abnormality of RBCs, low alveolar oxygen tension) you have adhesion that occurs to each other, leucocytes, and the endothelium causing vaso-occlusion and tissue hypoxia
- Inflammatory cytokines get released, which promotes inflammation of the airways



Pathophysiology of ACS cont.

- Role of vascular cell adhesion molecule 1 (VCAM1), which happens to be upregulated in the endothelium from a hypoxic state/fat embolism.
- The upregulation of VCAM1 has a role in inducing red cell adhesion to the respiratory endothelium and increasing vaso-occlusion within the pulmonary vasculature.

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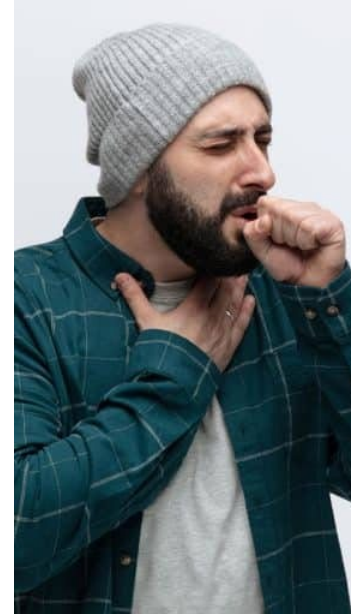


Picture 1 Sickled cells can clump together in the lungs, causing pain and trouble breathing.



Presentation and Diagnosis

- The presentation and severity associated with ACS can differ significantly in patients.
- ACS typically presents with chest pain, cough, dyspnea, fever, leukocytosis with new pulmonary infiltrate on imaging.
- Severe ACS can also present with rapid respiratory compromise and multi-organ failure
- Patient's can also present with neurological symptoms (AMS, seizures, etc).





Presentation and Diagnosis cont.

- Landmark study done by Vichinsky et al. in 2000, which was a multi-center prospective study
- Examined over 600 episodes of ACS in 538 patients and studied causes and outcomes in ACS in sickle cell disease.
- Identified a specific cause in 38% of patients, and when incomplete data was excluded identified in 70%.
- 2 main etiologies were fat embolism and infection (30%).

Causes and Outcomes of the Acute Chest Syndrome in Sickle Cell Disease

 [VIEW THE RELATED ARTICLE](#)

Published September 14, 2000 | N Engl J Med 2000;343:824 | DOI: 10.1056/NEJM200009143431122

[VOL. 343 NO. 11](#)

Presentation and Diagnosis cont.

- ACS (Adults/common etiologies)

- VOC
- Fat embolism

- ACS (Pediatrics/common etiologies)

- Infection
- Asthma

TABLE 4. CAUSES OF THE ACUTE CHEST SYNDROME.*

CAUSE	ALL EPISODES (N=670)	AGE AT EPISODE OF ACUTE CHEST SYNDROME		
		0-9 YR (N=329)	10-19 YR (N=188)	≥20 YR (N=153)
		no. of episodes (%)		
Fat embolism, with or without infection†	59 (8.8)	24	16	19
Chlamydia‡	48 (7.2)	19	15	14
Mycoplasma§	44 (6.6)	29	7	8
Virus	43 (6.4)	36	5	2
Bacteria	30 (4.5)	13	5	12
Mixed infections	25 (3.7)	16	6	3
Legionella	4 (0.6)	3	0	1
Miscellaneous infections¶	3 (0.4)	0	3	0
Infarction	108 (16.1)	50	43	15
Unknown**	306 (45.7)	139	88	79

Presentation and Diagnosis cont.

- Common pathogens in ACS
 - Mycoplasma pneumoniae
 - Chlamydia pneumoniae
 - Respiratory syncytial virus

- Antibiotic therapy is important to facilitate in these patients to provide optimal treatment.

TABLE 5. INFECTIOUS PATHOGENS ISOLATED IN 671 EPISODES OF THE ACUTE CHEST SYNDROME.*

PATHOGEN	No. OF EPISODES
<i>Chlamydia pneumoniae</i>	71
<i>Mycoplasma pneumoniae</i>	51
Respiratory syncytial virus	26
Coagulase-positive <i>Staphylococcus aureus</i>	12
<i>Streptococcus pneumoniae</i>	11
<i>Mycoplasma hominis</i>	10
Parvovirus	10
Rhinovirus	8
Parainfluenzavirus	6
<i>Haemophilus influenzae</i>	5
Cytomegalovirus	4
Influenza A virus	4
<i>Legionella pneumophila</i>	4
<i>Escherichia coli</i>	3
Epstein–Barr virus	3
Herpes simplex virus	3
Pseudomonas species	3
Adenovirus	2
Branhamella species	2
Echovirus	2
Beta-hemolytic streptococcus	2
<i>Mycobacterium tuberculosis</i>	2
Enterobacter species	1
<i>Klebsiella pneumoniae</i>	1
<i>Mycobacterium avium</i> complex	1
Salmonella species	1
<i>Serratia marcescens</i>	1
Total	249

*All infectious agents isolated during episodes of the acute chest syndrome are included.



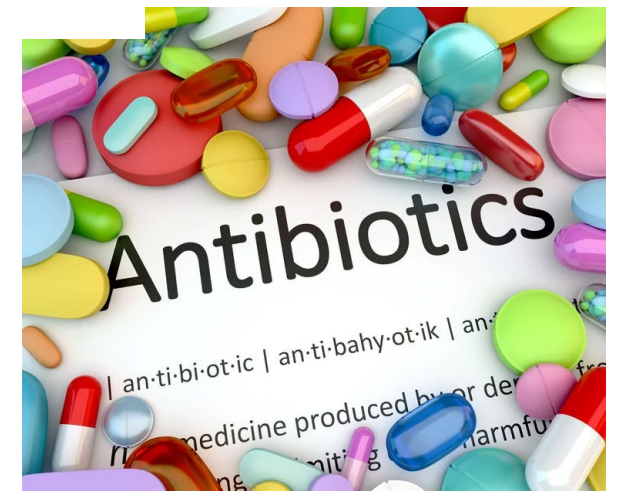
Presentation and Diagnosis cont.

- Diagnostic criteria
 - Acute illness w/new pulmonary infiltrate
 - 1 or more new respiratory symptoms or signs (cough, chest pain, fever, hypoxemia, wheezing, tachypnea).
 - Important to remember that these criteria are broad and to properly conduct a differential diagnosis (pneumonia, PE, pleural effusion, etc.)



Treatment of ACS

- Analgesia
- Antibiotic therapy
- Respiratory Support
- Fluid Management
- Blood Transfusion
- Early recognition and prompt initiation of treatment are associated with lower mortality rates, shorter hospital stays, decreased healthcare costs, and a reduced likelihood of recurrence

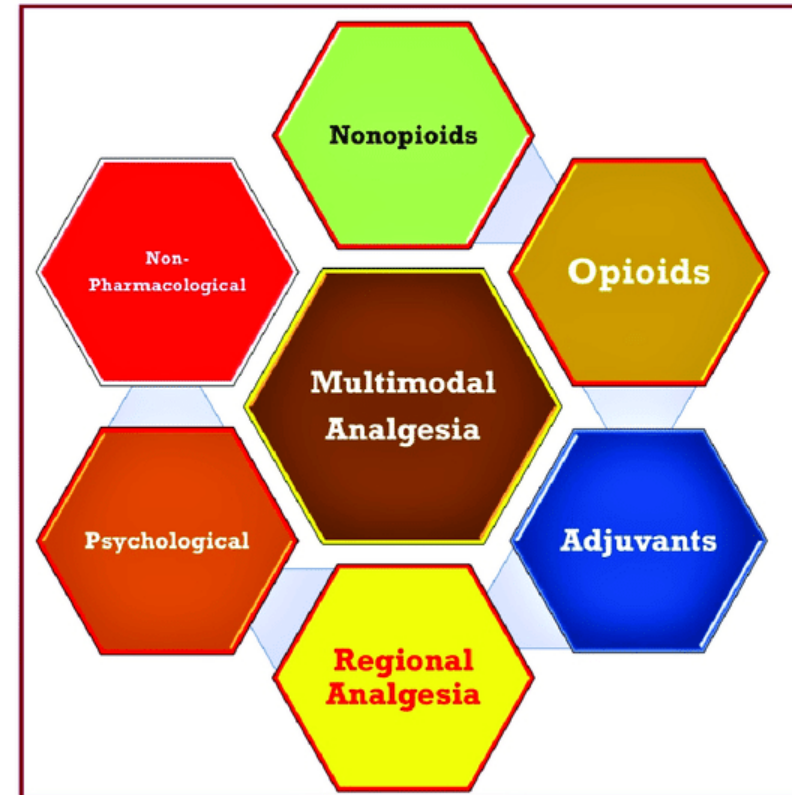


Treatment of ACS (Analgesia)

- VOC is a common trigger for ACS in patient's with SCD
- Utilization of multi-modal analgesia
- Evidence based guideline directed pain care (ASH guidelines)

Treatment of ACS (Analgesia) cont.

- VOC treatment
 - Opioids (pt specific protocol/weight-based regimen)
 - NSAID (Toradol x 5 days)
 - Acetaminophen
 - Pain dose ketamine (0.1-0.3mg/kg/hr, max dose 0.5-1mg/kg/hr)



Treatment of ACS (Antibiotic therapy)

- Infection is another common trigger for ACS
- Antibiotic therapy is important in patients with ACS
- Atypical organisms are common infectious agents in ACS
- Antibiotic therapy
 - 3rd generation cephalosporin (ex: Rocephin) with a macrolide (azithromycin) or fluoroquinolone (levofloxacin)
 - Critically ill patients can receive zosyn and vancomycin with a macrolide



Treatment of ACS (Respiratory Support)

- Respiratory support is important for this patient population
- If the patient is hypoxemic, supplemental oxygen should be administered to attain an O₂ saturation above 95% (nasal cannula, HFNC, NIPPV, mechanical ventilation if pt unable to protect airway)
- Incentive spirometry is another important aspect of ACS management. 10 maximal inspirations every 2 hours. IS helps to improve tidal volumes and also atelectasis.

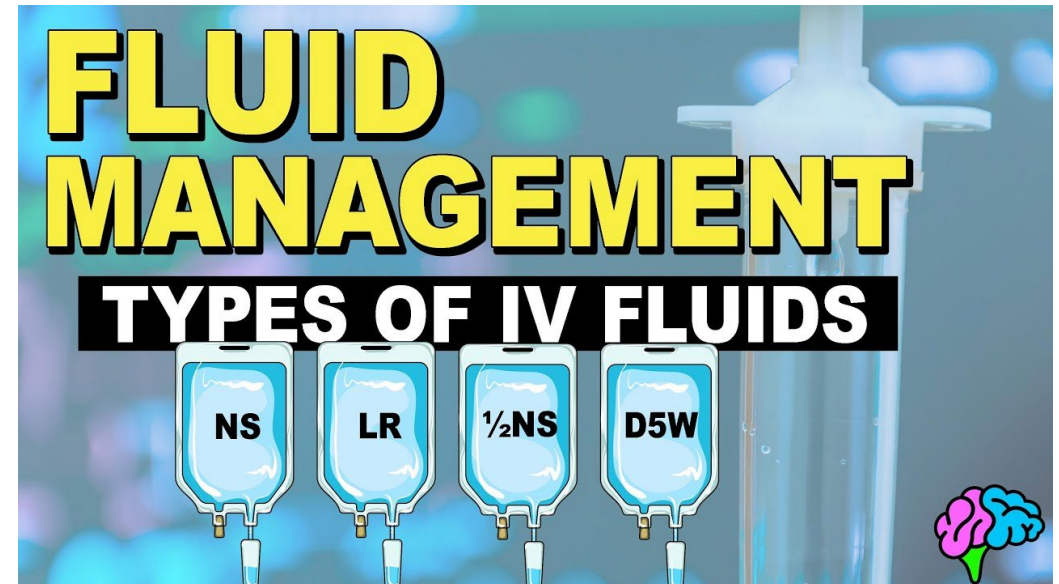


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Treatment of ACS (Fluid Management)

- Wang et al. discussed the importance of making sure fluid management is conservative and individualized for that patient, considering their fluid status.
- If the patient is euvolemic, maintenance fluids can be started (D5 in 0.45%NS) at maintenance rate to avoid over-hydration. In hypovolemic patient's fluid resuscitation should be employed.
- ASH guideline panel chooses not to offer a recommendation for or against IV fluids in addition to standard pharmacological management
- We need more high-quality studies regarding the efficacy and risk of IV fluids in treating ACS
- Fluid management should be guided by the patient's hydration status to restore and maintain adequate hydration without causing fluid overload.



Treatment of ACS (Blood Transfusion)

- Simple Transfusion
 - Symptomatic ACS
 - Hemoglobin <9 g/dL
 - Decrease in hemoglobin >1 g/dL from baseline

- Exchange Transfusion
 - Hypoxia despite oxygen supplementation
 - Worsening pulmonary infiltrates, increasing respiratory distress
 - Decreasing hemoglobin despite simple transfusion

- Target Hb >10g/dL for both simple and exchange. For adults, its recommended 1-2 units of RBC and 10ml/kg for pediatrics.



Knowledge Question #1

- What were the 2 most common pathogens that were isolated in ACS patients in Vichinsky et al. landmark study?
 - A. E.coli & Rhinovirus
 - B. Legionella pneumophila & RSV
 - C. Mycoplasma pneumoniae & Chlamydia pneumoniae
 - D. Streptococcus pneumoniae & Parvovirus

Knowledge Question #1 Answer

- What were the 2 most common pathogens that were isolated in ACS patients in Vichinsky et al. landmark study?
 - A. E.coli & Rhinovirus
 - B. Legionella pneumophilia & RSV
 - C. Mycoplasma pneumoniae & Chlamydia pneumoniae**
 - D. Streptococcus penumoniae & Parvovirus

Knowledge Question #2

- Which clinical scenario accurately describes the decision to utilize exchange transfusion?
 - A. Hemoglobin <9 g/dL
 - B. Decreasing Hypoxia after oxygen supplementation
 - C. Symptomatic ACS
 - D. Worsening pulmonary infiltrates, increasing respiratory distress

Knowledge Question #2 Answer

- Which clinical scenario accurately describes the decision to utilize exchange transfusion?
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 - C. Symptomatic ACS
 - **D. Worsening pulmonary infiltrates, increasing respiratory distress**

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