Pediatric Sickle Cell Disasters

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ACEP Scientific Assembly 2021

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General Approach – all patients

- Pain-coping behaviors in children and adults with sickle cell disease are not typical. Often they use distraction (e.g. eating, watching TV, using smart phone).
- For the stable patient, consider butterfly needles for blood draws, sparing veins from IVs (i.e. preserve veins whenever possible).
- Give supplemental O_2 only for hypoxia (blunts bone marrow response).
- Any and all organ systems may be affected: Neuro (stroke), ENT (infection), Pulm (pulmonary hypertension, acute chest syndrome), Cor (hypertension), GI (cholelithiasis/cholecystitis), GU (priapism), Heme (vaso-occlusive crisis), Musculoskeletal (osteonecrosis, osteomyelitis), etc.
- Evaluate for aplastic crisis with **CBC** (anemia) and **reticulocyte count** (bone marrow response). If anemic below baseline and a reduced reticulocyte count, (reticulocytes less than 1% or absolute reticulocyte count less than 10,000 per microL), consider **aplastic crisis**.

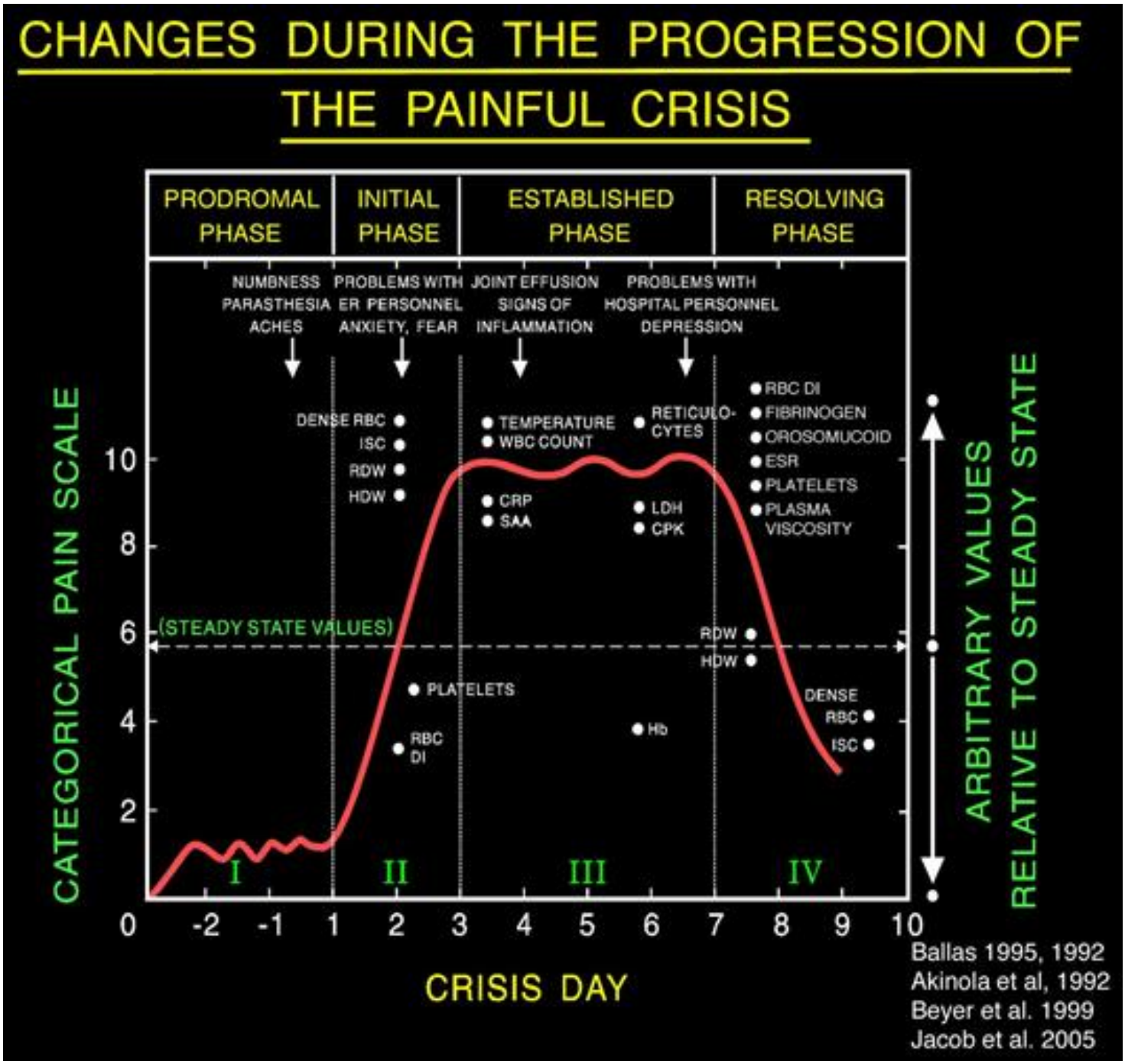
Background care

Pneumococcal vaccination – decreases the risk of invasive pneumococcal disease by up to 90%

Penicillin – prophylaxis due to asplenia; PCN BID in children less than 5 years of age drastically decreases pneumococcal risk. After age 5 years, there is a dramatic decline in the incidence of pneumococcal infection, probably because of a better immunologic response to encapsulated organisms such as *S. pneumoniae*.

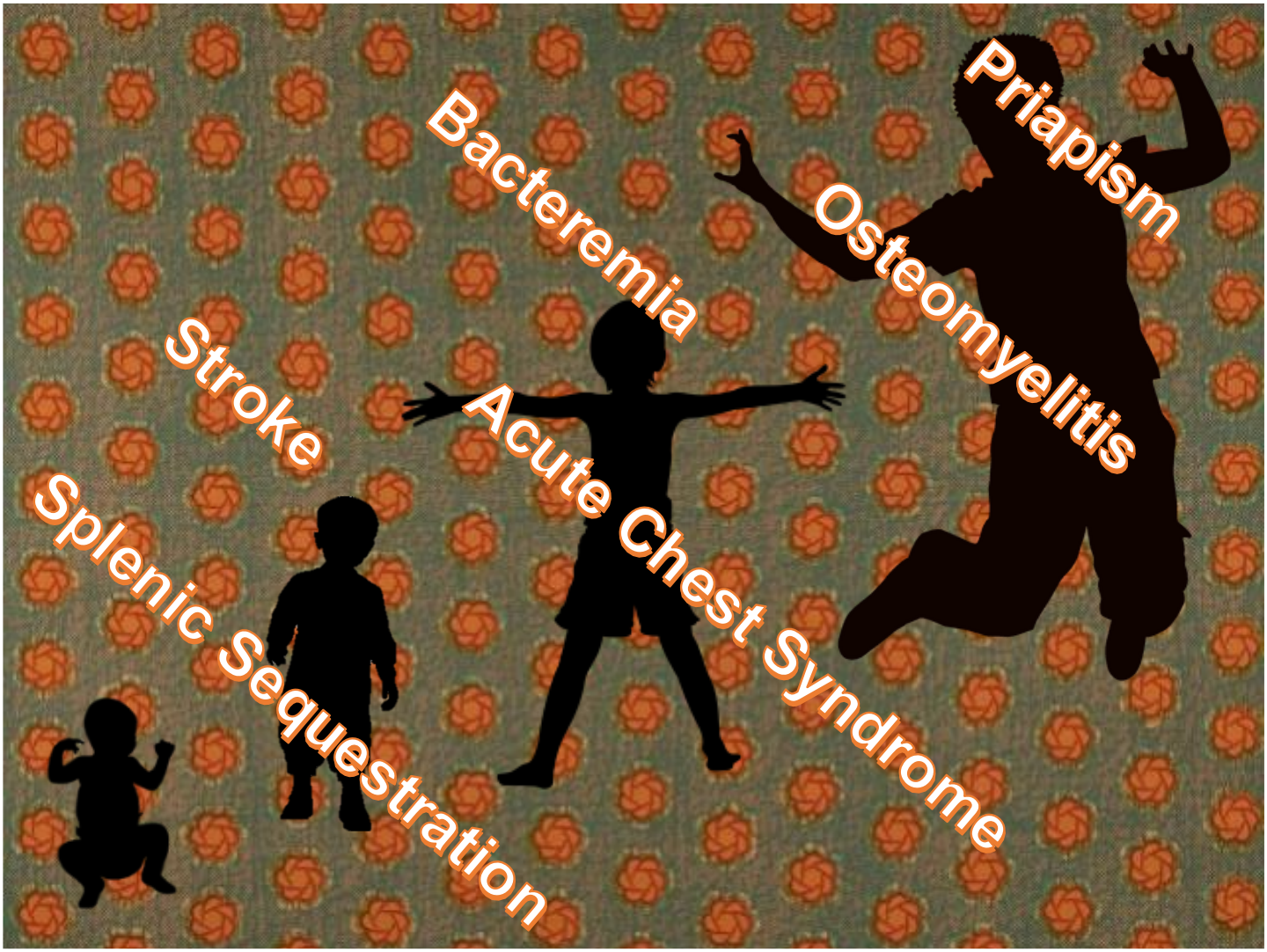
Folate supplementation – the average RBC lifespan in SCD is 12 days, compared to 120 days in non-affected individuals. More turnover (10 x) requires more substrate.

Hydroxyurea – promotes production of HbF, which is not susceptible to sickling as is HbS. Decreases morbidity, mortality. Less common side effects are neutropenia, bone marrow suppression, elevation of hepatic enzymes, anorexia, nausea, vomiting and infertility.



Ballas SK, Gupta K, Adams-Graves P. Sickle cell pain: a critical reappraisal. *Blood*. 2012; Figure 1.

Dangerous Complications of Sickle Cell Disease



Splenic sequestration – 5 months to 2 years (median is 18 months)

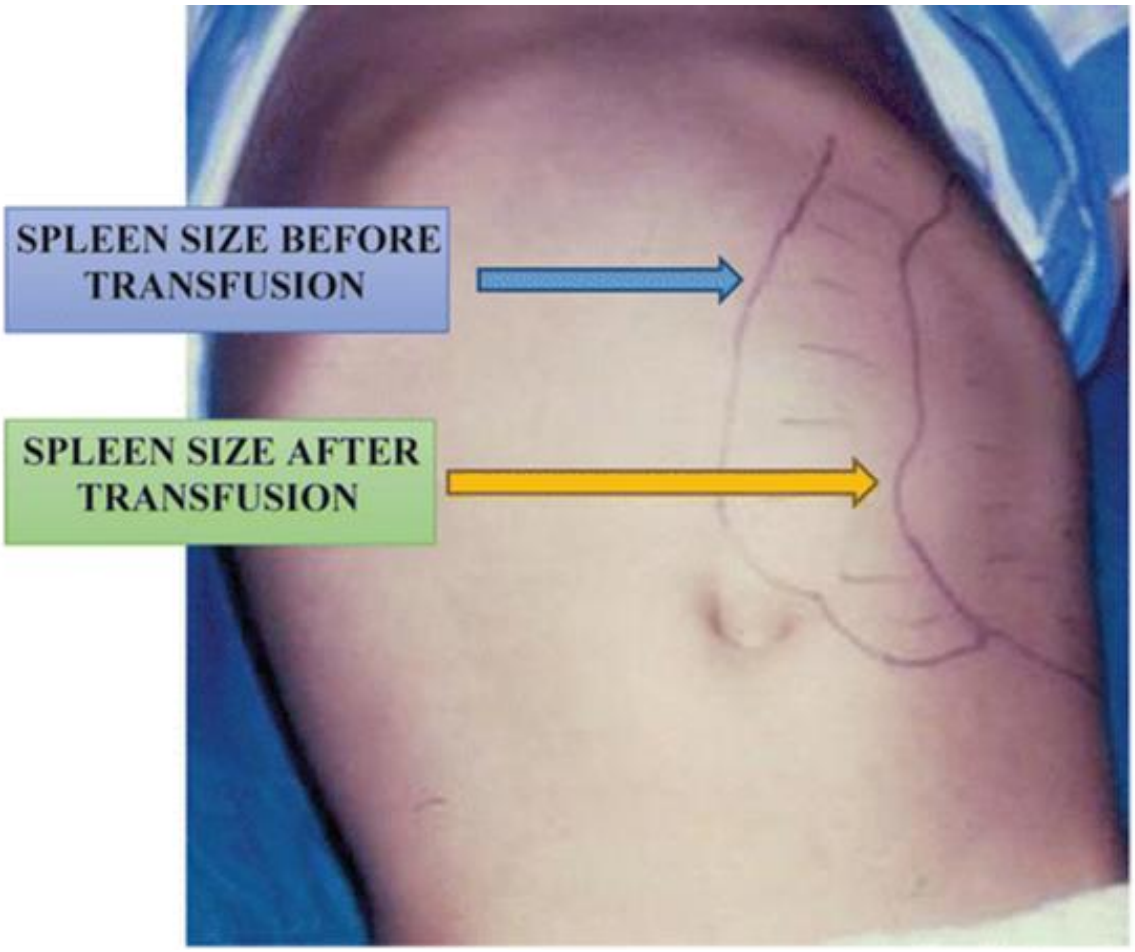
Presentation

- Occurs when RBCs flow *into*, but *not out of* spleen (RBCs pool and sickle).
- Present as rapidly enlarging spleen, an acute drop in hemoglobin by 2 g/dL. May result in shock and death.

Management

- Treat shock, transfuse PRBCs. Careful of re-perfusion syndrome, in which the perfused patient dumps damaged RBCs back into circulation.
- Splenectomy to prevent recurrence (untreated, 50% recurrence rate)

Sequestration crisis, transfusion, and patient's autotransfusion after perfusion restored:



Ischemic Stroke 2- 5 years old – up to 20% have silent brain infarcts

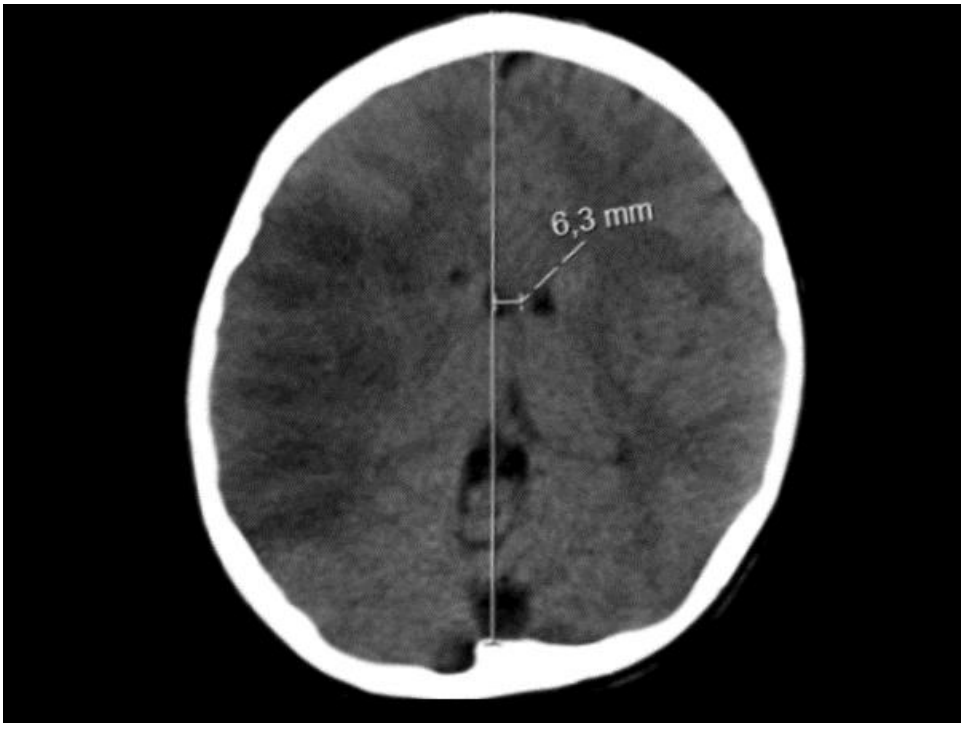
Infants may be screened for vasculopathy by transcranial doppler ultrasound and given regimen of regular blood transfusions to keep HbS levels below 30% (may reduce risk fi stroke by 90%).

Presentation

- May have baseline cognitive impairment, with or without evidence of infarct
- Usually present with focal neurologic deficits, often misinterpreted as having pain (e.g. “doesn’t want to move his arm”).

Management

- CT in ED, MRI as inpatient
- Transfusion goals: a) increase the hemoglobin concentration to approximately 10 g/dL and b) decrease the percentage of HbS RBCs to < 30%
- Start with simple transfusion PRBCs; possibly will need exchange transfusion
- Thrombolysis with tPA is not recommended for children < 18 years of age with ischemic stroke due to sickle cell (more important to treat cause; not FDA approved)
- Anticoagulation may be considered specifically for patients with cerebral venous sinus thrombosis.



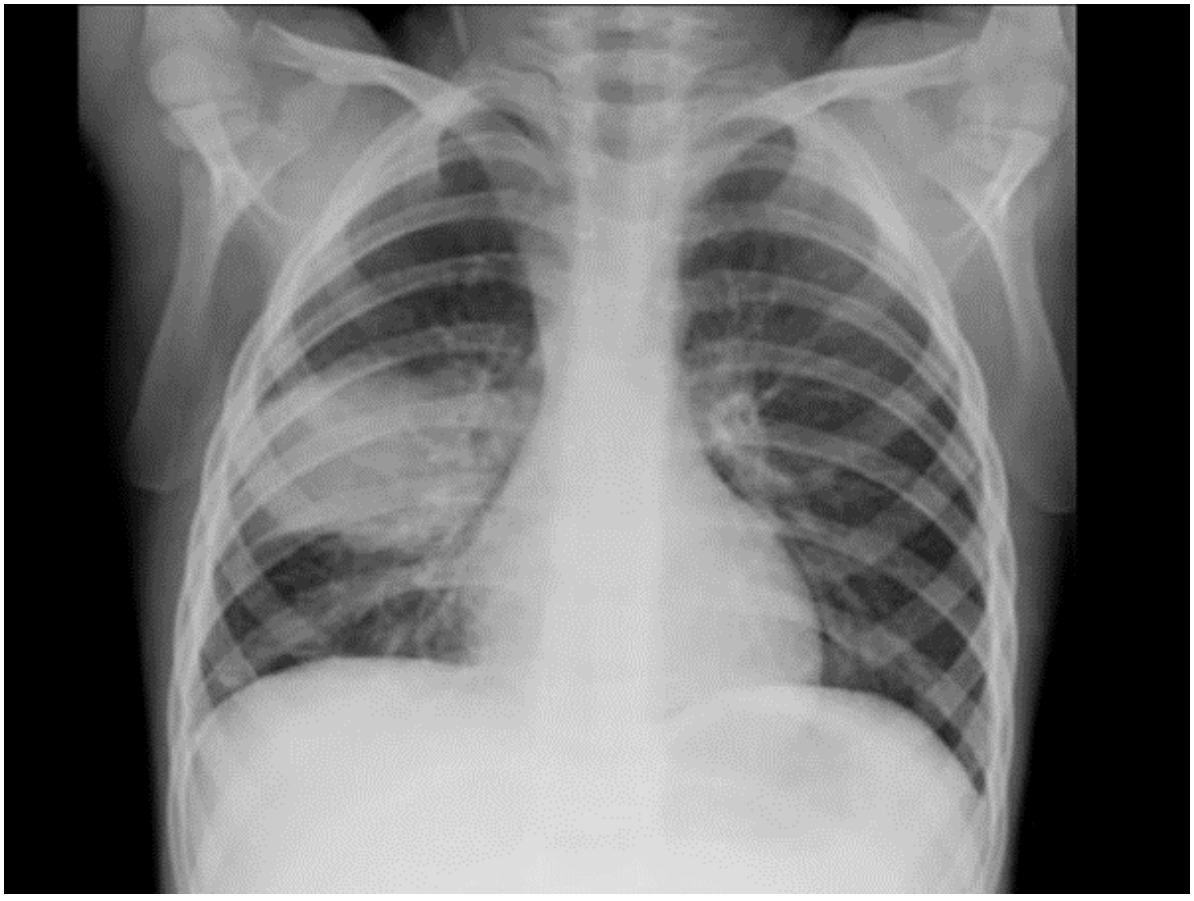
Acute Chest Syndrome – 2 to 4 years of age, some genotypes later

Presentation

- **New pulmonary infiltrate** with one other feature: fever, chest pain, shortness of breath, hypoxia
- 13% require mechanical ventilation, 3% mortality rate.

Management

- Supportive (pulmonary toilet, supplemental oxygen, non-invasive positive pressure ventilation, mechanical ventilation prn)
- IV antibiotics initially (nearly impossible to distinguish from pneumonia on presentation)
- Exchange transfusion in severe cases
- Dexamethasone may reduce need for serial blood transfusions



Fever/bacteremia – median age 6 to 7 years

Functional asplenia by age 4. Vaccines, prophylactic antibiotics (up to age 5) decrease morbidity/mortality. Patients always at risk for infection, bacteremia from encapsulated organisms and parasites.

Presentation

- Any fever in a child or adult with sickle cell is bacteremia until proven otherwise, regardless of results of viral respiratory panel results (co-infections and super-infections are common)

Encapsulated bacteria – *vaccine preventable*

- *Streptococcus pneumoniae* accounts for the majority (40-60% cases). Often symptoms are vague, fever, nausea, vomiting, diarrhea.
- *Haemophilus influenzae* type b often presents as bacteremia, pneumonia, and/or meningitis.
- *Neisseria meningitidis* is less common, and initially presents with vague flu-like symptoms. Rapidly progresses to septic shock, DIC, and purpura fulminans.

Encapsulated bacteria – *no vaccine available*

- Salmonella (food contamination), Klebsiella (opportunistic), Pseudomonas (opportunistic), Capnocytophaga (dog bites), Bordetella (respiratory variant and cats), Escherichia coli (food contamination)

Parasites and atypicals

- Babesia (tick-borne), Cytomegalovirus (opportunistic), Mycoplasma pneumoniae (respiratory), Mycobacterium tuberculosis (respiratory)

Management

- IV access, blood cultures, immediate empiric antibiotics, and admission.
- Ceftriaxone 50 mg/kg (bacteremia); 75 mg/kg (focal infection); 100 mg/kg (suspected meningitis) up to 2 g/kg.
- Vancomycin 15 mg/kg for suspected meningitis
- Clindamycin for cephalosporin allergy, 10 mg/kg

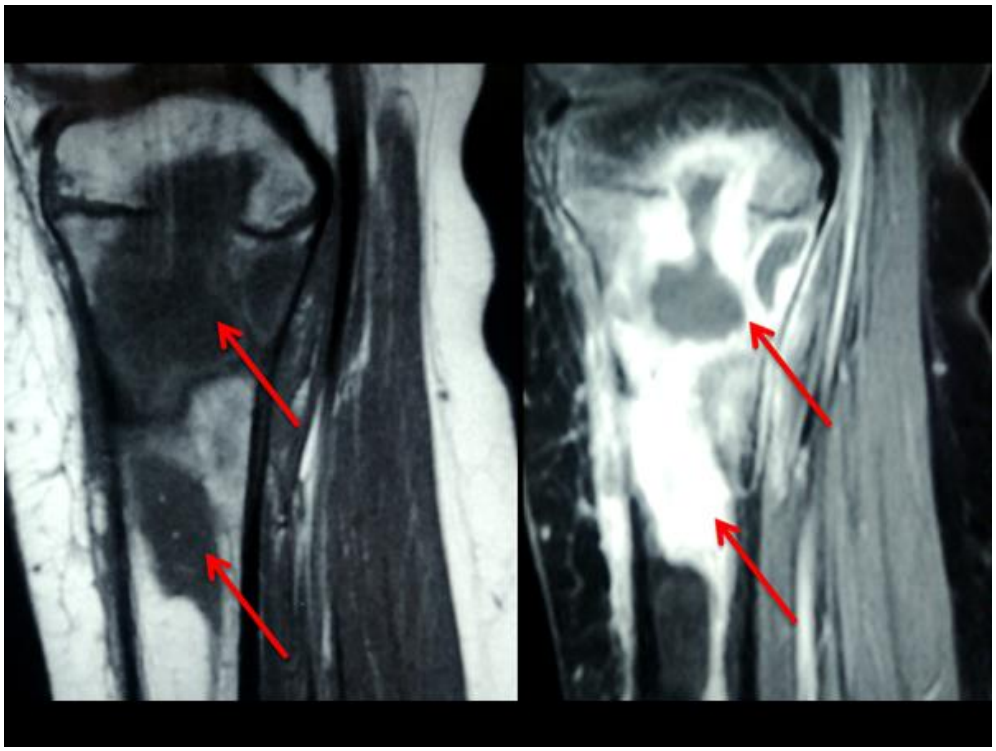
Osteomyelitis – 90% before 10 years of age

Presentation

- Difficult to distinguish osteomyelitis from vaso-occlusive crisis, and even osteonecrosis, as all can present with pain, inability to ambulate.
- Favoring osteomyelitis: fever, soft tissue edema, erythema, point tenderness to palpation.
- Encapsulated organisms are common.
- Avascular necrosis occurs in up to 10% of children with sickle cell disease. The natural progression of disease is: vaso-occlusion of supplying vessel which causes microfractures, collapse of cancellous bone, and finally collapse of the contour of the articular surface with chronic pain and loss of normal function.
- Interestingly, the entire epiphysis is often involved. Femoral heads are most common sites. Other common sites include humeral head and the distal tibia. Less common but important considerations are the mandible, elbow, and vertebrae.

Management

- Plain films, biomarkers (CBC, CRP, ESR)
- If concern for osteomyelitis, admission for MRI



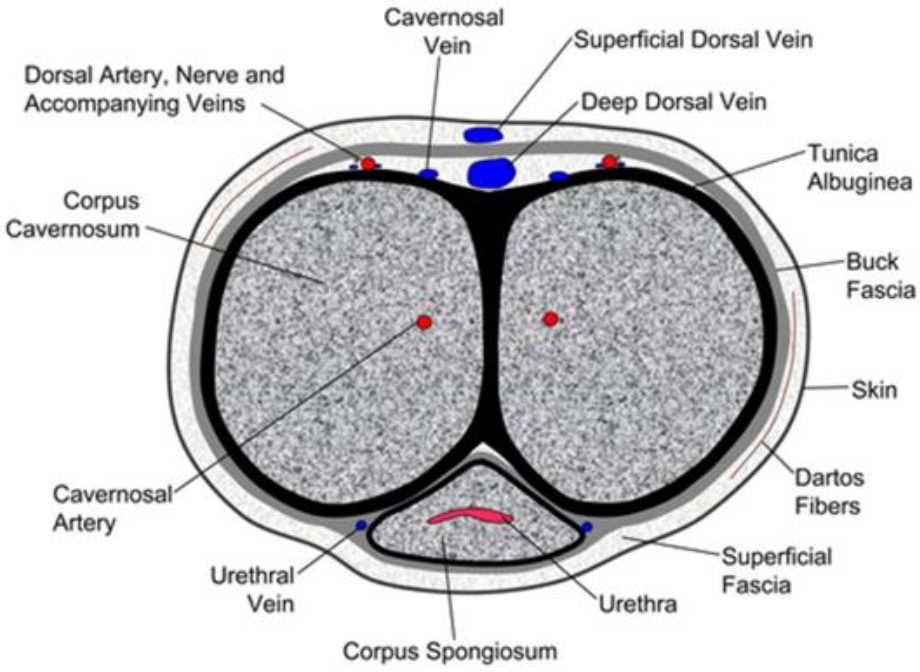
Priapism – mean 15 years of age

Presentation

- Common, possibly up to half of boys and men with sickle cell have experienced priapism (reporting bias).
- Majority of cases are low-flow, ischemic priapism.
- Often provoked by vaso-occlusive crisis, sexual activity, fever, dehydration, drug use, or associated with normal daily sleep-associated tumescence.

Management

- Fluids, pain control.
- If not rapidly controlled, needle aspiration, irrigation with phenylephrine (standard priapism aspiration/infusion technique)
- Exchange transfusion for refractory cases (although has not been proven to decrease time to detumescence)



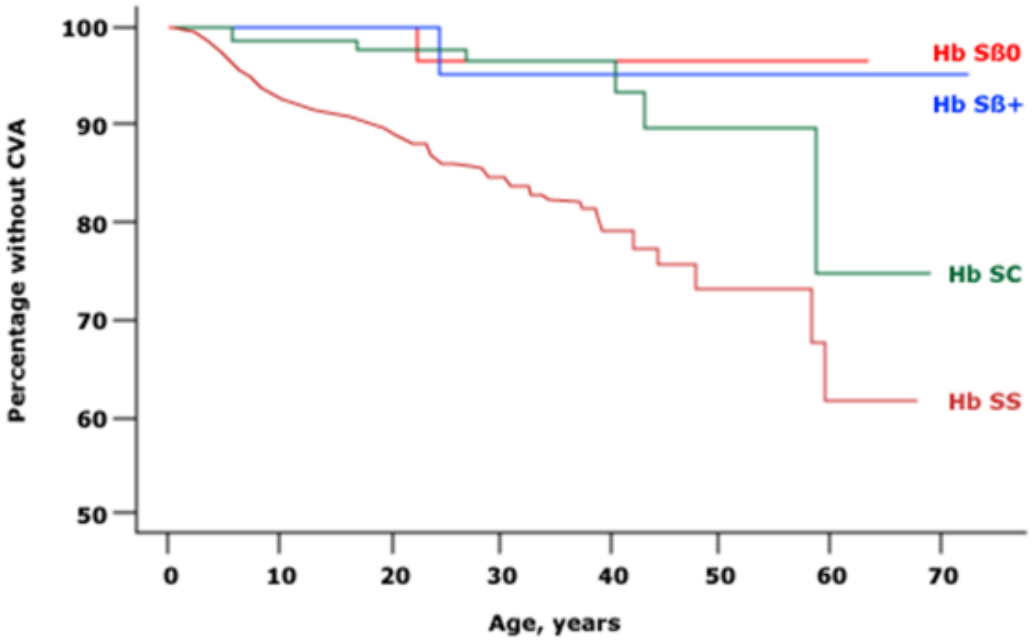
Hemorrhagic stroke – average age, adolescents throughout 20s

Presentation

- Intracranial hemorrhage is more likely in older adolescents and adults with sickle cell disease. Etiologies include hemorrhagic transformation of a previous ischemic stroke, or a primary subarachnoid, intraventricular, or parenchymal hemorrhage.
- Presentations vary and may be non-focal (severe headache) or typical (focal neuro deficits).

Management

- Reverse any previous anticoagulants
- Maintain platelet count above 100,000/microL
- Angiography as needed for culprit lesion
- Neurosurgical consultation
- Despite optimal treatment, mortality may be as high as 50%



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Specific Treatment Modalities

Analgesia

Typically sickle cell pain is managed at home with NSAIDs and sparingly with opioids. Patients who come to the ED often exhibit more morbidity and are opioid-tolerant.

Options include:

- Intranasal Fentanyl 2 mcg/kg
- Morphine 0.1 mg/kg/dose every 15-30 min titrated to effect
- Hydromorphone 0.015 mg/kg/dose every 15-30 min titrated to effect
- Ketamine 0.3 mg/kg (subdissociative dose) as an adjunct

Simple Red Blood Cell Transfusions

Goal is to dilute HbS red blood cells with functional HbA red blood cells to interrupt cycle of hypoxia, sickling, and occlusion.

For severe complications, may start with simple PRBCS transfusion of 5-10 mL/kg. Careful in potential sequestration (see above)

Exchange Transfusion

Goal is to replace patient's blood manually (traditional, time- and effort-consuming) or by automated **erythrocytapheresis** (more effective, especially with large volumes) . Used when goal is to decrease Hb S concentration to less than 30%

Iron Chelation

Each unit of packed red blood cells can introduce approximately 250 mg of elemental iron. This is usually of concern in patients with chronic routine transfusions or recurrent need for acute transfusion.

Iron overload can cause cardiac, liver, and endocrine disorder. Serum ferritin levels give an estimate of total body stores and may be used to drive therapy. Various chelating agents are available; deferoxamine is common.

Hydroxyurea

Discharged patients should be evaluated for the need for hydroxyurea therapy, as it can reduce the incidence of acute chest syndrome, transfusion requirement, and mortality when compared with those on placebo. It is typically indicated for most children, and for adults with recurrent pain episodes.

For further reading on Ghanian folktales:

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