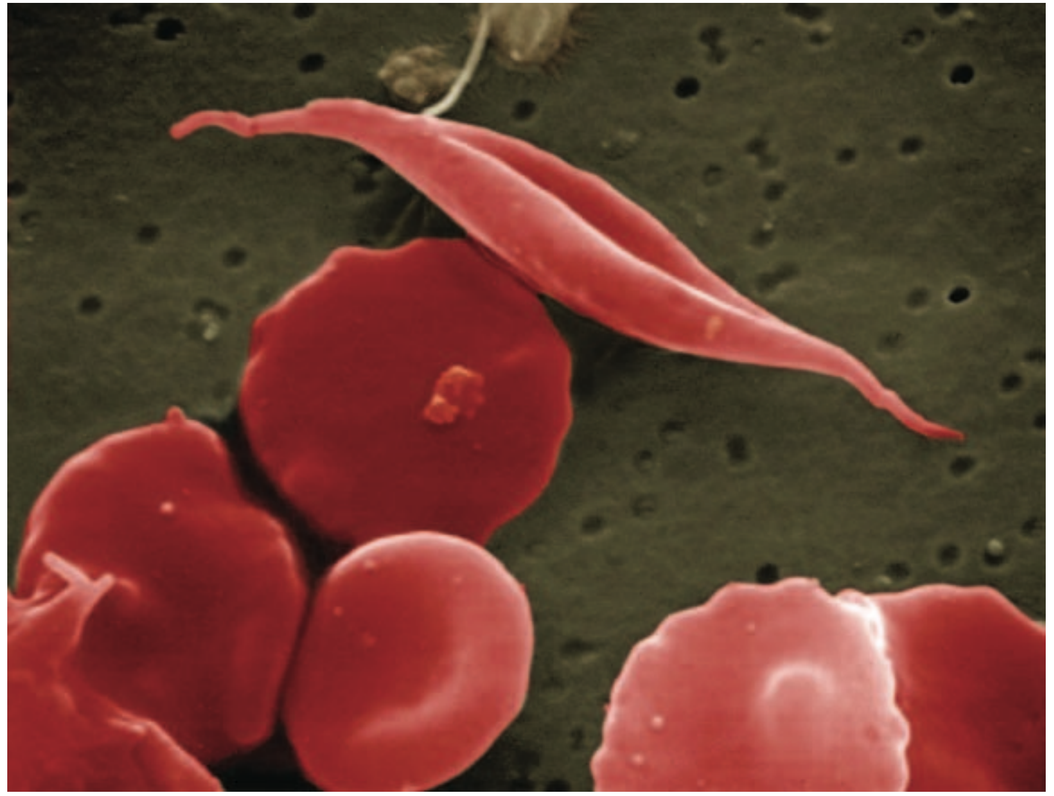
Sickle Cell Disease Emergencies

Harbor-UCLA PEM Curriculum



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General Information

Epidemiology

- ~2 million Americans have a mutation, ~100,000 with full SCD. Most common in African American and Black community but seen in all races. Larger populations in Middle Eastern, and Mediterranean communities.
- On Newborn screen so early surveillance and preventative measures can be started
- 90% survive to adulthood, but lifespan 2-3 decades shorter than unaffected people

General Information

Genetics

- Genetic disease: substitution of valine for glutamic acid on hemoglobin beta chain molecule → HbS (molecule at risk for polymerization, creating sickle shaped blood cells)
- Homozygote HbSS is disease state. Combinations with other hemoglobin mutations also can be symptomatic as Sickle Cell Anemias (SCA). Sickle Cell Disease (SCD) refers to all the disease genotypes

SEVERITY

Genotype	Name/Classification	SCD/SCA classification	Baseline Hb (g/dL)	Baseline HbS % (hemoglobin electropheresis)
HbAA	Normal	None	Normal	0
HbAS	Sickle Cell Trait, carrier	None	Normal	<40%
HbSS	Sickle Cell Disease	SCA, SCD	6-9	>90%
HbSβ^0	HbSβ^{0-}thalassemia (compound heterozygote)	SCA, SCD	7-9	>80%
HbSβ^1	HbSβ^{1-}thalassemia (compound heterozygote)	SCD	9-12	>60%
HbSC	Hemoglobin SC (SCD)(compound heterozygote)	SCD	9-14	50%

Mainstays of HbS Treatment

Disease surveillance and preventative care

- **Newborn screen** for Sickle Cell
- **Routine vaccination** + 23 valent PCV (@2y/o & 5y/o), MCV (@2y/o, booster q5y), MenB (@10y/o)
- **Hydroxyurea** (PO, daily):
  - Main mechanism: Increases circulating HbF (fetal Hb)
  - Reduces number pain crises, acute chest, number transfusions, cost benefit
  - Not recommended in pregnancy
  - Adverse effects: **myelosuppression** (pts have CBCs monitored; improve with lower dosage)
- **Penicillin prophylaxis** (BID, age 0-5 y/o). Continued longer if invasive pneumococcal infection OR splenectomy
- **Stroke prevention and surveillance**
  - Transcranial doppler (TCD) monitoring (ICA and MCA vessels)
  - If abnormal TCD, scheduled transfusions to maintain a goal Hb and %HbS
- **Eye Health:** Retinopathy in ~50%
- **Kidney Health:** urine screens for proteinuria, risk for papillary necrosis
- **Screening echos:** development pulmonary hypertension ~10% pts

Vaso-Occlusive Crisis (VOC)

AKA Pain Crises

Definition/Pathophysiology	Severe pain. Hallmark complication of SCA (HbSS and HbSβ^0) Sickling of rbcs → vaso-occlusion → ischemic pain
Presenting s/s	Severe pain (often sudden onset, but can be gradual) Extremities, chest, back are most common locations *__Dactylitis__ in infants/toddlers (6-18mo): metacarpal/tarsal bones with swelling (refusal to walk, irritable) – declines as hematopoiesis shifts to long bones
IMPORTANT	**TRUST PATIENTS IN THEIR PAIN AND TREAT IT AGGRESSIVELY** No VS, exam findings, labs can confirm or deny this
Labs	**No labs specifically rule VOC in or out!** (lab eval for consideration of other complications)

Vaso-Occlusive Crisis (VOC) Cont.

Management/Supportive Care

Triage	ESI 2 for immediate room and rapid assessment Door to analgesic time ideally <30 mins! Protocols can help
Pain Management	VOC is classified as Acute (not chronic pain): Opiates useful 1. Follow personalized pain management plan (if pt has) 2. NSAIDS if no contraindication (often already done) 3. IV Opiates (most pts know what dose they need/chart review). If unable to get IV access, SubQ better than IM. Consider IN fentanyl until get IV access • **Frequent re-eval pain control every 15-30 mins** • Escalate doses by 25% until good analgesia • Manage side effects of meds (itching, nausea) prn. Encourage PO meds 4. Provide non-pharmacologic pain management (heat, distraction, massage) 5. Monitor for over sedation, consider EtCO2 monitoring
Hydration	Bolus only if hypovolemic mIVF if not tolerating PO No need to over-hydrate
O2	O2 only if <95% Room air
Blood transfusion	Only if meets transfusion requirements (not mainstay of VOC treatment)

Vaso-Occlusive Crisis (VOC) Cont.

Disposition

Consultation	Pediatric hematology/oncology Some centers have a hemoglobinopathy specific clinic or specialist	
Disposition	DISCHARGE	Pain controlled well with few IV doses meds Pts and families will tell you when comfortable Need hematology follow-up plan
	ADMIT	Concern for other complication of SCD Difficult to control pain requiring multiple doses IV pain meds Dispo decision after ~6-8hrs care max During admission, encourage incentive spirometry (preventative for acute chest syndrome) Shared decision making with pt/family/heme team
Hydration	Bolus only if hypovolemic mIVF if not tolerating PO No need to over-hydrate	
O2	O2 only if <95% Room air	

Fever in SCD

ED Evaluation

Specific Concerns to consider	**Risk SBI** (↓splenic fxn) with encapsulated bacteria such as *S. pneumoniae* Penicillin prophylaxis and pneumococcal vaccinations do reduce incidence Target H&P to **find fever source**. Consider these potential invasive infections:	
	• Acute Chest Syndrome • Osteomyelitis • UTI	• Cholangitis • Sepsis • Meningitis
Labs	• **CBC with diff** • **Reticulocyte count** • **Blood culture** • Consider viral testing if resp Sx	• UA/UCx • Consider LFTs • Consider LP if concern meningitis
Imaging	• CXR or lung US if respiratory symptoms or chest pain (Acute Chest Syndrome) • XR extremities with point tenderness or pain + redness/swelling (may need advanced imaging for osteomyelitis)	

Fever in SCD

Management and disposition

Consultation	Pediatric hematology/oncology Some centers have a hemoglobinopathy specific clinic or specialist	
Antibiotics	Empiric dose broad spectrum antibiotic like Ceftriaxone IV x1 at least Treat any infections found as indicated (e.g. amoxicillin for AOM)	
Disposition	DISCHARGE	Well appearing Need hematology follow-up plan
	ADMIT	T≥39.5* (expert consensus) Age consideration (Harbor recommends admit <2 y/o) Unwell-appearing (including if Hb significantly below baseline) High concern SBI based on workup findings (ie WBC >30*) Uncertain/poor follow-up

* Individual institutional cutoffs may vary

Priapism

Definition/Pathophysiology	Sustained, unwanted erection >4hrs ~35% males may experience “low flow” priapism (rigid shaft, soft glans)
Management	Full details of management under GU emergency section 1. Pain control (systemic, or consider dorsal penile block), ketamine? 2. Hydration (PO or IV if unable) 3. Cold pack 4. Aspiration
Transfusion?	2014 Consensus statement doesn’t recommend PRBC or exchange transfusion for acute management (mod rec; low quality evidence)
Consultations	Urology if conservative management unsuccessful

Hepatobiliary disease

Presentation and workup

Pathophysiology	Hemolysis → unconjugated bilirubin → form sludge and stones	
Prevalence	Cholelithiasis in ~10% children 2-4 y/o ~40% by age 14-15 ~70% by adulthood	
At risk for…	• Cholecystitis • Choledocholithiasis	• Acute Hepatic Sequestration (AHS) (like splenic sequestration but in liver) • Acute Intrahepatic Cholestasis (AIC) (AKA Sickle Cell Hepatopathy)
s/s	Abdominal pain (esp RUQ), nausea, vomiting, jaundice	**AHS:** Acute upper abdominal pain Acute hepatomegaly associated **AIC:** Acute RUQ pain, jaundice, hepatomegaly, **acholic stool**

Hepatobiliary disease

Findings and management

	Cholelithiasis and cholecystitis	**Acute Hepatic Sequestration and Acute Intrahepatic Cholestasis**
Labs	LFTs: cholestatic pattern CBC: leucocytosis	• CBC: ↓Hb by 2 in AHS, thrombocytopenia in AIC • LFTs: severe hyperbilirubinemia in AIC, cholestatic pattern • Abnormal synthetic function: thrombocytopenia, hypoalbuninemia,coagulopathy • Coags: (coagulopathy common in AIC)
Imaging	**RUQ ultrasound** (POCUS OK to start) with stones	RUQ US: no sign obstruction
Management	Surgical consultation Alert hematologist	• Hydration, pain control • Hematology consultation (maybe GI as well) • Simple or exchange transfusion in confirmed cases (discuss with hematology)
Disposition	ADMIT if req acute surgery or not tol PO DISCHARGE (after discussion with surgery and hematology if tolerating PO and pain controlled)	ADMIT

Aplastic Crisis

	Acute Anemia **Aplastic Crisis is an important cause**	
s/s	Fatigue (gradual), shortness of breath, syncope, pallor, sometimes fever. VS: tachycardia At risk high output heart failure	
DDx	**Aplastic crisis:** Parvovirus B19 infection of erythrocyte precursors → ↓rbc production, ↓rbc lifespan	**Other causes acute anemia** • Sequestration (spleen, liver, lungs) • Hemolysis (e.g. delayed transfusion rxn) • SCD related renal injury (papillary necrosis) • Non-SCD process (e.g. GI bleed)
Labs	**CBC:** Acute anemia = Hb 2 g/dL below baseline or <6 if unknown baseline **Reticulocyte count:** ↓ (aplastic crisis), normal or↑ in other etiologies **Type & Screen**	
Management	**Transfuse** PRBC to improve symptoms/hemodynamics (need not return to baseline Hb) If Aplastic crisis, Place on droplet precautions (viral infection)	
Consult/Dispo	Hematology ADMIT	

Splenic Sequestration

Important cause of acute anemia

s/s	Rapidly enlarging abdominal mass (splenomegaly - blood collects there), sometimes pain Typically children 1-4 y/o (before splenic involution) Sudden weakness, pallor, tachycardia or in shock with splenomegaly HbSC and HbSβ+ may experience later in life and more subacute presentation LUQ pain in older pt can be splenic infarction
Labs	**CBC:** Acute anemia = Hb 2 g/dL below baseline or <6 if unknown baseline - ↓plts, ↓wbc possible (get stuck in spleen too with the rbcs) **Reticulocyte count:** ↑ **Type & Screen**
Management	IV fluid hydration **Transfuse** small aliquots PRBC (3cc/kg, accounting for *auto-transfusion*) to goal Hb ~8 Over-transfusion is risk for hyper-viscosity (stroke risk) especially as sequestered re-enter circulation
Consult/Dispo	Hematology ADMIT
Prognosis	Recurrences possible (families instructed to follow spleen size) Recurrences, or chronic hypersplenism may require splenectomy

Acute Chest Syndrome

#1 cause death in SCD, #2 reason hospitalization

Definition	New CXR finding + fever, cough, chest pain, resp distress, hypoxia Often have triggering illness, surgery, or VOC event Pt w/asthma or previous ACS episode higher risk
Pathophysiology (Multifactorial)	**Infection** (viral or bacterial - chlamydia and mycoplasma associated) **Embolic** (marrow fat), **Sickling** and occlusion, **Atelectasis** (ie too much sedation - incentive spirometry as preventative) **Edema**
Imaging	**CXR:** new opacity (often RUL but also can be multifocal). CXR findings may lag **Lung US:** sub pleural consolidations (smaller lesions identifiable earlier)
Labs	**CBC/Retic:** Hb often somewhat below baseline **Type & Screen** Otherwise, labs non-specific **Blood culture** if febrile Consider viral studies

Acute Chest Syndrome Cont.

Management and disposition

Management	- **Empiric antibiotics** such as IV Ceftriaxone + PO macrolide (azithromycin) - **Supportive care:** Bronchodilators, respiratory support, incentive spirometry while awake, pain control (but avoid over-sedation) - **PRBC transfusion** if Hb <9 or >2 below baseline (improve O2 carrying capacity) - **Gentle IV fluids:** usually 3/4 maintenance rate (one institutional guideline) - **Exchange transfusion (urgent not emergent)** in setting of worsening of respiratory failure despite supportive care, progressive anemia despite simple transfusion, (discussion with hematology; usually inpatient procedure)
Consult/Dispo	Hematology ADMIT, may require PICU care
Prognosis	May become critically ill! Progressive, more diffuse disease (multifocal opacities) → progression to multi organ dysfunction Recurrent episodes can lead to chronic lung disease

Acute Stroke

Epidemiology	10% prevalence among HbSS pts. Can occur at any age Estimated more ~35% have silent infarcts Many will have recurrent events
Presentation	Acute onset neuro deficit (hemiparesis, CN palsy), speech change (dysphasia or aphasia), severe headache, Can also present with seizure or altered mental status, coma Highly suspect stroke in SCD pt with neuro symptoms! Often preceded by TIA event Acute Chest Syndrome, Acute Anemia, Aplastic Crisis may precipitate stroke
Pathophysiology	Most commonly ICA or MCA stenosis or occlusion
Imaging/Labs	Activate “code stroke” Noncontrast Head CT (look for hemorrhage), then MRI/MRA CBC, Retic, T&S
Management	PRBC Transfusion to goal HbS < 30% (keep Hb <11 until confirmed HbS level) Exchange Transfusion (discuss w/heme and critical care) Consult with hematology and neurology ADMIT to PICU (consider transfer to pediatric stroke center)

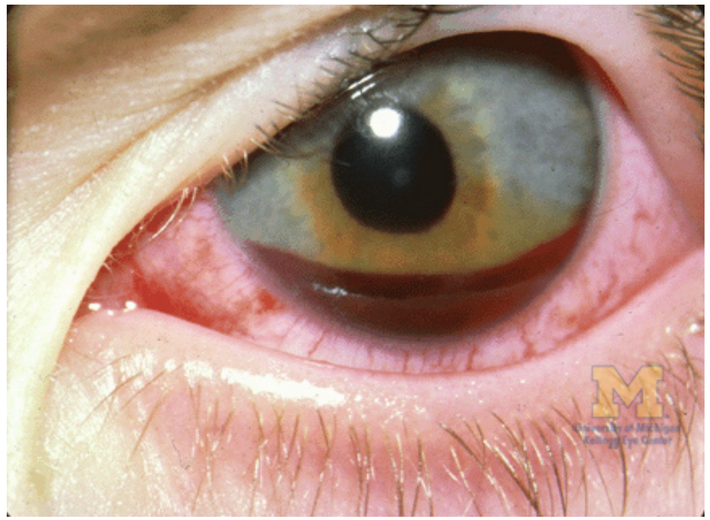
Ocular Emergencies: pretty much all bad

Take vision and eye complaints seriously and call ophtho

Disease Entity	Clinical Presentation	Pathophysiology	Interventions
Hyphema	Blood layering in anterior chamber after **ocular trauma, vision change** *Can affect Sickle Cell Trait too!	Blood in ant chamber → sickling → obstruction → ↑IOP (prolonged presence → other complications, vision loss)	Possible "anterior chamber parasintesis" or hematoma evac
Vitreous hemorrhage, Retinal detachment	Vision change, flashers, floaters	**Acute:** Secondary to trauma or **Chronic:** 2/2 **sickle cell retinopathy** (HbSC particularly, and early onset)	Ophtho: possible laser or surgical options
Orbital infarction	**Pain, proptosis,** swelling, **vision change,** pain with eye movements, entrapment	Orbital bone VOC → infarction of structures within orbit → swelling and pain DDx: orbital cellulitis, osteomyelitis	ED action: CT orbit, consider abx Ophtho: poss surgery
Central Retinal Artery Occlusion	Painless acute blindness	Thrombotic event or 2/2 prolonged hyphema and ↑IOP	Stroke eval ?Exchange Transfusion

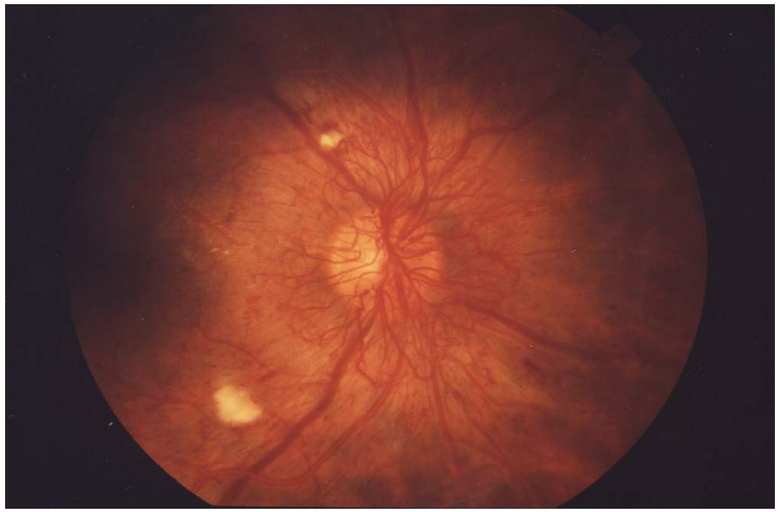
Ocular complication images

Hyphema



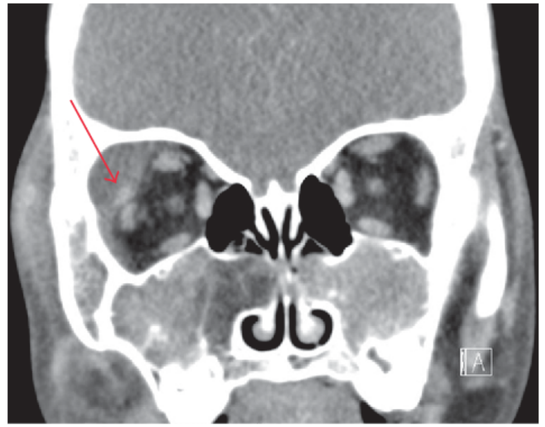
http://kellogg.umich.edu/theeyeshaveit/trauma/hyphema.html

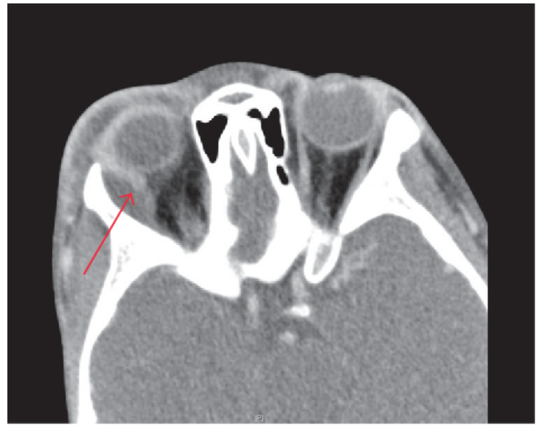
Retinopathy



http://www.nei.nih.gov/photo/eyedis/index.asp

Orbital infarction





McBride, Cameron L et al. “Orbital Infarction due to Sickle Cell Disease without Orbital Pain.” Case Reports in Ophthalmological Medicine 2016 (2016): n. pag.

Ocular complications are serious!

Consult an ophthalmologist for vision change, eye pain, swelling, or trauma!

Transfusion Indications

Be mindful

- Avoid unnecessary transfusions
  - Pts at high risk alloimmunization (development of antibodies)
    - Can make it very difficult to match blood long term
- Balance risk/benefits (benefit in stroke prevention)
- Discuss your plans with hematology

Social Considerations

Racism in medicine

- Avoid the term “sickler”
  - Considered offensive to many patients with SCD
  - Associated with negative attitude toward this patient population
- Long history of mistreatment and undertreatment by medical system
- Listen to The Realness to hear about the rapper Prodigy’s life with Sickle Cell

The Future

- Wider use hematopoietic stem cell transplant
- More precise genotyping and phenotyping
- Gene therapy
- **New therapies**
  - Crizanlizumab: monoclonal antibody against P-selectin, ↓cell adhesion, ↓VOC
  - Voxelotor: increase Hb affinity to O2 and inhibit polimerization

- **More research overall**

Take-aways

- Be familiar with SCD management: PCN, hydroxyurea, vaccination, screenings
- Treat Sickle Cell Pain aggressively
- Take fever, abdominal pain, and eye symptoms seriously
- Be mindful about blood transfusions
- Don’t hesitate to consult hematology
- Check your implicit biases

References

Read:

U.S. Department of Health and Human Services. (2014). *Evidence based management of sickle cell disease*. 77. https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report 020816_0.pdf

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