Sickle Cell Disease

I. Epidemiology

a. Inherited genetic disorder characterized by an abnormality of hemoglobin that predisposes to polymerization and consequent deformation
b. Found primarily in African, Mediterranean, Indian, or Middle Eastern heritage
c. In the US, 1/500 African Americans are homozygous
d. 20-30% of all sickle cell deaths occur before age 5 with the highest mortality rate between 1-3 years old
e. Significantly decreased life span
f. Due to infections
g. Prevention and treatment of infections has lead to reduction in early mortality

II. Vasoocclusive Crises

a. General

i. Due to polymerization of deoxygenated HbS
ii. RBC's deformed
iii. Causes microvascular sludging and obstruction
iv. Initially reversible, but not after several episodes of sickling
v. Most common reason for ER visits
vi. Painful events
    1. Back
    2. Extremities
    3. Chest
    4. Abdomen
vii. The average sickle cell patient experiences 4 "attacks" per year
viii. What are some triggers for pain crises?
    1. Stress (emotion/physical)
    2. Cold Exposure
    3. Dehydration
    4. Hypoxia/ High Altitude
    5. Infections (esp. viral in children)
ix. Most crises occur in the absence of an identifiable trigger!!!
x. Often associated with low-grade fever and leukocytosis
xi. Any temp >101.1F or a abs band count >300 cells is more likely to represent an infectious etiology for the crises

b. Musculoskeletal

i. Due to infarction of bone, viscera, and ST
ii. Pain can recur in the same location or different locations
iii. Usually involving the long bones
    1. Femur
    2. Tibia
    3. Humerus
    4. Lumbosacral region

c. Peds Vasoocclusive Crises

i. **Sickle Dactylitis**: avascular necrosis of the metacarpals and metatarsals secondary to vasoocclusion of the nutrient arteries of the bone marrow cavities.
    1. Most common peds presentation of SCD
    2. Present > 6 mo due to fetal hemoglobin
    3. Usually < 2 yrs old and rare after age 5
    4. Swelling of the hands and feet usually associated with a low grade fever

d. Avascular Necrosis of the Femoral Head

i. Localized pain to the hip and difficulty weight bearing/ ambulating
ii. Bilateral Hip XRs useful in identificaiton
iii. Conventional X-ray film of right hip shows irregularity of femoral head with increased density and flattening of the articular surface consistent with an avascular necrosis of the femoral head with concomitant joint space narrowing and degenerative changes

e. **Acute Chest Syndrome**

i. Leading cause of death in SCD in the US
ii. *Definition*: Fever and worsening of respiratory symptoms accompanied by new pulmonary infiltrates on CXR
iii. Thought to be due to pulmonary infarction
iv. *Pt Presentation*: Pleuritic CP, cough, dyspnea, hypoxia, tachypnea, and leukocytosis
v. *W/U*: CXR, Pulse Ox, ABG, CBC and Retic count
vi. Infiltrates may be in
    1. One lobe
    2. Diffuse and bilateral
    3. Thought to be due to infection of a pulmonary infarct
vii. Pleural effusions may also be present
viii. XR findings delayed by hours or days
ix. Follow with serial CXR's
x. Tx of Acute Chest Syndrome
    1. P_{AO2} 70-80 mmHg, SaO2 92-95%
        a. O_2 2-4 L/min
    2. P_{AO2} <70 mmHg, SaO2 <90%, worsening A-a gradient, or 10% drop from baseline
        a. Ventilatory support
        b. Transfusion therapy
    3. Supportive
    4. Pain Control
    5. Hydration
    6. +/- Antibiotics

f. CNS Crises

i. Usually acute onset hemiparesis, seizures, headaches, TIAs, vertigo, sensory hearing loss, CN Palsies, Paresthesias, and coma.
ii. Usually painless but abrupt in onset
iii. Evaluation with a Head CT or Brain MRI
iv. Tx of CNS Crises
    1. Acute Ischemic Stroke

a. Thrombolytic Therapy as indicated
b. Hydration
c. Exchange Transfusion
d. Seizure Control
e. Maintain Normoglycemia
f. Treat Hypothermia

2. TIAs
   a. Exchange Transfusion if the pt has significant large vessel disease
   b. Antiplatelet therapy
3. SAH
   a. Neuro/Peds ICU
   b. Exchange Transfusion to < 30% HbS
   c. Nimodipine

g. <u>Abdominal Pain</u>

i. Abrupt onset, *<u>lack of localization</u>*, and recurrence.
ii. PE is usually normal (no peritoneal signs)
iii. Most likely due to Mesenteric, Hepatic, or Splenic infarction
iv. Diff Dx: any pathologic process that causes belly pain

h. <u>RUQ Abdominal Pain</u>

i. Biliary Colic, cholelithiasis and/or cholecystitis
ii. Due to bilirubin gallstones from increased RBC turnover
iii. 30-70% of all SCD pts have bilirubin gallstones
iv. Only ~10% become symptomatic

i. <u>RUQ Syndrome</u>

i. Abrupt onset RUQ pain, anorexia, Bili >50 and progressive hepatomegaly.
ii. Usually benign and self limited in peds but may lead to liver failure in adults (rare)
iii. Thought to be due to cholestasis
iv. Eval by RUQ U/S or CT Abd
v. Tx: usually reversible with IVF and other supportive measures

j. <u>Renal Events</u>

i. Common but generally asymptomatic
ii. Flank pain, renal colic, CVA tenderness
iii. Gross or microscopic hematuria
iv. May have renal tissue in the urine due to papillary necrosis
v. Consistently monitor renal function in SCD pts

k. Vasoocclusive Crises

l. <u>Priapism</u>

i. Painful, sustained erection
ii. Severe, prolonged attacks can cause impotence
iii. Seen in up to 30% of SCD males
iv. <u>Tx of Priapism</u>
   1. IV Hydration
   2. Tx may be by oral administartion of α-adrenergic agonists, intrapenile injection of vasodilators, or needle aspiration of the corpora cavernosa

3. Exchange transfusion if > 2-3 hrs duration
4. Urology Consultation

m. <u>Tx of Vasoocclusive Crises</u>

i. Pain Management
1. Morphine and Diamorphine (UK)
2. Avoid meperadine
3. Opioid tolerance and physical dependence are expected with long-term opioid Tx and should not be confused with psychologic dependence
4. PCA's may be needed
5. NSAID's have an additive effect
6. Aggressive to ease pain and enable patients to attain maximal functional ability
7. Tailored to each pt
8. More guidelines at
a. www.aafp.org/afp/20000301/practice.html

ii. Hydration with IVF
iii. Supplemental Oxygen
iv. Pain Med Guidelines for SCD in Children
1. Use the IV route
2. Morphine 0.1-0.15 mg/kg IV
3. Hydromorphone 0.02-0.05 mg/kg IV
4. ¼ to ½ the loading dose in 15-30 min intervals
5. Titrate to pain relief, pain intensity, mood, and sedation

III. Hematologic Crises

a. Anemia
i. Abnormal shape causes decreased life span of the RBC
ii. Chronic Hemolytic Anemia
iii. Acute drop in serum HgB
iv. Generalized weakness
v. Malaise
vi. Fatigue
vii. Shortness of breath
viii. Dyspnea on exertion
ix. Progressive CHF
x. Shock

b. <u>Acute Splenic Sequestration</u>

i. Infants and young children
ii. 2nd most common cause of death in kids with SCD
iii. Splenomegaly and hypovolemic shock
iv. Often preceded by a viral infection (parvovirus B19)
v. Increased Retic counts due to compensation for anemia
vi. Major
1. Spleen rapidly enlarges
2. HgB drops to < 6 g/dL or 3 g below pt baseline

vii. Minor
1. Insidious

2. HgB usually > 6 g/dL

viii. Transfusion of PRBCs and exchange transfusion

c. Hematologic Crises

d. <u>Aplastic Crises</u>

i. Bone marrow erythropoiesis slows or stops completely

ii. Fatigue, dyspnea, H/A, anemia

iii. ***<u>Hgb 1-3 g/dL, Hct <10%</u>*** and Retic counts as low as 0.5%(*)

iv. WBC and plts normal

v. Tends only to occur once in a pts life

vi. Precipitating Factors

1. Parvovirus B19
2. Folic Acid
3. Iron Deficiency
4. Marrow toxic drugs

vii. Transfusion of Packed RBCs is necessary due to the severe anemia

IV. <u>Infection Crises</u>

a. <u>Osteomyelitis</u>

i. Pt presents with acute bone pain

ii. Blood, subperiosteal, or joint cultures obtained prior to starting Abx

iii. XR Films show radiolucency

iv. Abx coverage for *Salmonella spp*. Due to increased incidence

b. Infections

i. At risk of developing serious infections

ii. Pts develop functional asplenia

iii. Sepsis from encapsulated organisms

1. Most common cause of death in children is sepsis from *Strept. Pneumoniae*

iv. Prevention

1. Pneumovax at 24 months age
2. Prophylactic penicillin therapy
3. H. influenza vaccine

v. <u>Fever of Unknown Origin in Sickle Cell</u>

1. Temp >101.3F is a serious emergency
2. CBC, CXR, UA, Pulse Ox, Blood Cx, Urine Cx, Throat Cx
3. Consider inpatient treatment with IV Abx
4. Outpatient treatment if
    a. Stable for >4 hours after initial IV Abx
5. Close follow up arranged within 24 hours

V. <u>Specific Therapies for SCD</u>

a. <u>Transfusion Therapy</u>

i. In pts with splenic sequestration, severe aplastic crisis, CVA, priapism, Acute Chest Syndrome, and Pregnancy

ii. If the pt is stable, Hgb > 6 and retic count >20, transfusion therapy may be avoided

iii. Goal to reduce HbS containing RBC to < 30% of RBC's

iv. Avoid transfusing to HCT > 36

v. Transfuse if
    1. Heart failure
    2. Dyspnea resistant to O2 Therapy
    3. Fatigue
    4. Hypotension resistant to IVF bolus
vi. Consult a hematologist is transfusion is necessary

b. <u>Hydroxyurea (Hydrea)</u>

i. Used to increase % Hgb F
ii. Prevents the polymerization of HgS
iii. Can decrease # of hospitalizations and # of crises in adults
iv. Not approved for children

VI. <u>Cochrane Review</u>

a. "Currently, pain is inadequately managed"
b. Objective
    i. assess the effectiveness of pharmacological analgesic interventions for pain management in sickle cell disease
c. Criteria
    i. All RCT's involving pharmacological tx of acute or chronic pain in children or adults with SCD were selected from January 1965 through to June 2002
    ii. 9 studies identified
    iii. All studies involved small numbers of patients with acute sickle cell pain only
    iv. NSAIDs, Opiates, and Corticosteroids
d. Authors Conclusions
    i. Limited evidence with under powered studies
    ii. No difference in the efficacy of sustained-release oral versus parenteral morphine
    iii. Consider oral morphine??
        1. *Roxanol 10-30 mg PO q 4*
    iv. Parenteral corticosteroids appear to shorten the period over which analgesics are required and hospital length-of-stay

VII. <u>Disposition</u>

a. <u>Inpatient</u>

i. Pt requiring hospitalization
    1. Temp >101.3F
    2. WBC >30,000 with left shift
    3. Hematologic parameters significantly altered from baseline
    4. Respiratory distress, hypoxia, or lobar infiltrates on CXR
    5. New CNS findings
    6. Splenic sequestration or Aplastic Crisis
    7. Acute Abdomen
    8. Prolonged Priapism
    9. Crisis not responsive to IV hydration and analgesia
    10. Intractable pain
    11. Inability to maintain adequate oral hydration
    12. Follow up is uncertain

b. <u>Outpatient</u>

i. Outpatient instructions
ii. Good oral hydration
iii. Pain meds
iv. Return if fever >100.4F, worsening pain, or vomiting
v. Follow up with PCP within 24 hours

VIII. Questions

a. Question 1

i. What is the most common presentation of SCD in Peds pts?
1. Avascular Necrosis
2. Osteomyelitis
3. Sickle Dactylitis
4. Acute Chest Syndrome

b. Question 2

i. What bacteria should be considered as a possible etiology of osteomyelitis in SCD?
1. Staphylococcus aureus
2. Steptococcus pneumoniae
3. Salmonella spp.
4. Hemophilus influenzae

c. Question 3

i. Pts with functional asplenia are at risk of developing sepsis from encapsulated organisms. How can we prevent this?
1. Vaccinations
2. Prophylactic Antibiotics
3. Spleen Transplant
4. Place pt in a bubble

d. Question 4

i. The goal of transfusion therapy is to decrease HbS in the blood to less than what percentage?
1. 10
2. 20
3. 30
4. 40

e. Answers

i. 3
ii. 3
iii. 1,2
iv. 3