Management of Sickle cell Disease

- During hospitalization
  - Hydration
  - Thromboembolism prophylaxis
    - Hepapin
    - LMWH
    - Fondaparinx
  - Splenic sequestration
    - Features
      - Large, tender spleen
      - Drop in Hb by 2 g/dL
      - Thrombocytopenia
      - Reticulocytosis
    - Hydration
    - Blood transfusion
      - 50%
      - reduce risk of hyperviscosity syndrome
- Infection prevention
  - Immunization
    - Pneumococcal
    - Influenzae
    - MEningococcus
  - Prophylactic penicillin
    - Penicillin V BD
      - until 5 yrs
    - Erythromycin if penicillin allergy
- Nutrition
  - Folic acid
  - Multivitamins
    - No iron
  - Vitamin D
- Pain Management
  - Acute pain episode
    - aggressive pain relief
    - opioids etc
    - Blood transfusion if haemodynamically unstable
  - Chronic pain
    - Leg ulcers
    - Avascular necrosis
- Transfusion therapy
  - lowers % HbS
    - Dilution of HbS via the addition of HbA from the blood of normal donors
    - decreases levels of HbS
      - Suppress erythropoietin release secondary to fall in Hb
      - reduce production of new RBC containing HbS
      - longer circulating lifespan of HbA containing normo
  - Therapeutic
    - Acute stroke
    - Acute chest syndrome
    - Acute multiorgan failure
    - Symptomatic anemia
  - prophylactic
    - primary/ secondary stroke prevention
    - Pre op
  - phenotypically matched units
  - Leucoreduction
    - prevent CMV infection
    - prevent febrile non hemolytic transfusion reactions
- hydroxyurea
  - reduces incidence of painful crises
  - prolongs survival

Sickle cell crisis is a medical emergency

Routine Evaluations
BP (stroke)– Annually
Transcranial Doppler (annually)
Retinal evaluation after 10yo
Pulmonary hypertension/ Baseline pulmonary evaluation– wheezing, SOBOE, persistent cough
priapism
Family planning, birth control
Leg ulcers – prevention

LABS
FBC– mild to moderate Anemia, sickled cells, Polychromasia (reticulocytosis); Howell-Jolly Bodies (hyposplenia)
Normochromic/ normocytic unless thalassaemic or iron deficiency
Hbf moderately high
Hb electrophoresis
Severe anemia if splenic sequestration crisis, aplastic crisis (associated with parvovirus B19 infections), hyperhemolytic crisis

The evolution of pain is also associated with changes in the levels of CRP, fibrinogen, serum lactate dehydrogenase, interleukin-1, tumor necrosis factor, and serum viscosity

Peripheral blood smear from a patient with sickle cell anemia. The blood smear shows sickled red cells (S), a target cell (T), findings consistent with functional asplenia, including a nucleated red blood cell (upper left), a red blood cell containing a Howell-Jolly body (black arrow), and Heparin cells (red arrow).
Courtesy of Carole Lee Hoff, DO (2005).

Normal peripheral blood smear. Several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen. The red cells are of relatively uniform size and shape, with a central area of pallor that occupies approximately one-third of the cytosol of the cell (cytoplasm, central pallor (red arrow) should equal one-third of its diameter.
Courtesy of Carole Lee Hoff, DO (2005).

Peripheral blood smear

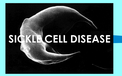
PROGNOSIS/ SURVIVAL
Survival of individuals with SCD is reduced compared with those without SCD, but the prognosis for SCD has been steadily improving following the institution of comprehensive care that includes **newborn screening, immunizations, antibiotics, hydroxyurea, and more rapid prevention and treatment of disease complications (eg, stroke).** In regions where comprehensive care is available, the disease has shifted from a fatal pediatric illness to a chronic disease often associated with progressive deterioration in quality of life and organ function

–Half survived beyond the fifth decade
–The median age at death for those with homozygous sickle Hgb (HgbSS) was 42 years for men and 48 years for women.
–The median age at death for those with HgbSC disease was 60 years for men and 68 years for women.

- Clinical
  - Acute painful episodes (Sickle Cell Crisis)
    - Precipitated by
      - weather
      - infection
      - Menses
      - Alcohol consumption
      - nocturnal hypoxemia
      - obstructive sleep apnoea
    - Any part of body
      - back
      - chest
      - extremities
      - Abdomen
    - premonitory symptoms
      - episodes last 2-7 days
      - more frequent pain- higher mortality in pt >19yo
      - First symptom in disease
  - Growth and development
    - Delayed puberty
    - Growth failure
      - weight > height
  - Retinopathy
    - Haemorrhage
    - Renal artery occlusion
    - Retinal detachment
    - proliferative retinopathy
  - Pulmonary
    - Acute chest syndrome
      - infiltrate with pulmonary symptoms
        - Pneumonia
        - Infarction
        - Fat embolism
        - bone marrow infarction
        - thrombosis
      - initial negative CXR
      - fall in Hb and platelet count
      - Rise in phospholipase A2
  - Renal
    - asymptomatic albuminuria
      - Progressive renal disease
        - Renal failure
      - (occlusion of vasa recta capillaries in renal medulla)
  - Priapism
    - impotence
  - Pregnancy
    - Fetal
      - Miscarriage
      - IUGR
        - low birth weight
    - Maternal
      - acute chest syndrom
      - Bacteriuria
        - UTI
      - pyelonephritis
      - Endometritis
      - Thromboembolic events
  - Dermatologic
    - Leg ulcers
    - Myofascial syndromes
    - Acute hepatic ischemia
  - Hepatobiliary complications
    - Acute hepatic ischemia
    - benign cholestasis
    - Hepatic aequestration crisis
    - Transfusional iron overload
    - Acute and chronic cholelithiasis secondary to pigmented gallstones
    - Acute ancd chronic liver disease
      - hepatitis C infection
      - complicates blood transfusion
    - Drug toxicity
  - Cardiac complications
    - Increased cardiac output
    - Myocardial infarction
    - LVH
    - Arhythmias
      - prolonged QT
      - first degree AV block
    - Cardomegaly and left/ right heart failure
  - Bone complications
    - accelerated hematopoiesis/ bone infarction
    - chronic hemolysis
      - Chronic skull tower
      - Frontal bossing
      - Flat mouth deformity of vertebrae
      - osteoporosis
    - Vitamin D deficiency
    - Bone marrow infarction
      - reticulocytopenia, exacerbates anemia; leukoerythroblastic blood picture, pancytopenia
      - Pulmonary fat embolism
        - Anemia in children with SCD is most commonly caused by S. pneumoniae (62-65). Bacteremia typically presents with leukocytosis, a left shift in the differential count, aplastic or hypoproliferative crisis due to associated bone marrow suppression, sometimes disseminated intravascular coagulation, and is associated with a mortality rate of 20 to 50 percent (56). The risk of recurrent S. pneumoniae sepsis and death is increased in patients who have had previous sepsis
        - exchange blood
        - heparin
        - Pteroids
      - Orbital compression syndrome
        - Headache
        - Fever
        - Palpebral edema
  - Infection
    - Bacteremia
      - Splenic dysfunction
      - Encapsulated organisms
        - 1. Strep pneumoniae
        - 2. Haemophilus influenzae
      - Dysfunctional IgG adn IgM responses
      - Defective alternative complement fixation pathway
      - Opsiophagocytic dysfunction
    - Meningitis
      - Strep pneumoniae
    - Bacterial pneumonia
      - Mycoplasma pneumoniae
      - Chlamydia pneumoniae
      - Legionella
      - Respiratory viruses
    - Osteomyelitis
      - Long bones/ multiple sites
        - Salmonella enterica
        - Staphylococcus
  - hypospenism/ functional asplenia
    - due to repeated episodes of splenic infarcts
    - correlates with more Howell- Jolly Bodies and membrane vacuoles
  - Psychosocial issues
    - Poor family relationships
    - Social isolation
    - low self esteem
      - anxiety/ depression
    - withdrawal from normal daily living
    - neurocognitive impairment
  - Multiorgan failure
    - potentially fatal
    - prompt and aggressive exchange transfusion therapy
  - Neurological
    - 24% experience clinical **stroke** by 45 yo
      - TIA
      - Cerebral infarcts
      - Intracerebral haemorrhage
      - Spinal cord infarction/ compression
      - Vestibular dysfunction
      - Sensory hearing loss
    - risk of neurocognitive decline and intracranial haemorrhage
      - increase with age
    - Epilepsy
      - 2-3x more common
      - 40% increased all-cause mortality
    - Chronic transfusion therapy
      - Overt CNS injury
      - Abnormal transcranial doppler screening

Sickle cell disease describes all conditions associated with sickling; sickle cell anemia describes homozygosity for HbS

Autosomal Recessive Inheritance
Homozygosity for HbS (results from substitution of ***valine for glutamic acid*** in the 6th amino acid of β globin chain)– poorly soluble when deoxygenated– marked decreased in red cell deformability



Vaso-occlusive phenomena and Hemolysis