Sickle Cell Disease (SCD)

- Background
  - Hemoglobin S is the result of a mutation resulting in a substitution of valine for glutamine at 6\textsuperscript{th} position in beta globin chain
  - Autosomal recessive inheritance
Substitution of Valine for glutamine at 6th position in beta globin chain, due to mutation on chromosome 11.

Hypoxemia
Dehydration
Acidosis

HBS polymerizes when deoxygenated

Irreversible sickling
Vaso-occlusion
Dactylitis
Autosplenectomy
Acute chest syndrome
Pain crisis
Renal papillary necrosis

HbF

Protective in the 1st few months of life

Aggregate → needle-like structures

Extravascular and Intravascular hemolysis

Anemia
Jaundice (unconjugated)
Increase the risk of gall bladder stone
Decreased haptoglobin
Target cells

Extramudular hematopoiesis
Clinical manifestations of sickle cell disease

**Anaemia**
- All have moderate anaemia (usually Hb 6–10 g/dl) with clinically detectable jaundice from chronic haemolysis

**Infection**
- All have marked increase in susceptibility to infection from encapsulated organisms such as pneumococci and *Haemophilus influenzae*. There is also an increased incidence of osteomyelitis caused by *Salmonella* and other organisms. This susceptibility to infection is due to **hyposplenism** secondary to chronic sickling and **microinfarction** in the spleen in infancy. The risk of overwhelming sepsis is greatest in early childhood.

**Painful crises**
- **Vaso-occlusive crises** causing pain affect many organs of the body with varying frequency and severity. A common mode of presentation in late infancy is the hand-foot syndrome, in which there is dactylitis with swelling and pain of the fingers and/or feet from vaso-occlusion (Fig. 22.9). The bones of the limbs and spine are the most common sites. The most serious type of painful crisis is acute chest syndrome, which can lead to severe hypoxia and the need for mechanical ventilation and emergency transfusion. Avascular necrosis of the femoral heads may also occur. Acute vaso-occlusive crises may be precipitated by exposure to cold, dehydration, excessive exercise or stress, hypoxia or infection.

**Acute anaemia**
- Sudden drop in haemoglobin from:
  - **Haemolytic crises** – sometimes associated with infection
  - **Aplastic crises** – haemoglobin may fall precipitously. Parvovirus infection causes complete, though temporary, cessation of red blood cell production
  - **Sequestration crises** – sudden splenic or hepatic enlargement, abdominal pain and circulatory collapse from accumulation of sickled cells in spleen
Priapism

Needs to be treated promptly with exchange transfusion as it may lead to fibrosis of the corpora cavernosa and subsequent erectile impotence

Splenomegaly

Common in young children, but becomes much less frequent in older children

Long-term problems

Short stature and delayed puberty

Stroke and cognitive problems – although 1 in 10 children with sickle cell disease have a stroke, twice that number develop more subtle neurological damage (Fig. 22.10), often manifest with poor concentration and school performance

Adenotonsillar hypertrophy – causing sleep apnoea syndrome leading to nocturnal hypoxaemia, which can cause vaso-occlusive crises and/or stroke

Cardiac enlargement – from chronic anaemia

Heart failure – from uncorrected anaemia

Renal dysfunction – may exacerbate enuresis because of inability to concentrate urine

Pigment gallstones – due to increased bile pigment production

Leg ulcers – uncommon in children

Psychosocial problems – difficulties with education and behaviour exacerbated by time off school may occur
Figure 22.9  Dactylitis in sickle cell disease.
Figure 22.10 MRI of the brain in sickle cell disease showing multiple cerebral infarcts.
Figure 22.11 Chest X-ray in acute sickle chest syndrome showing bilateral lower zone consolidation. (Courtesy of Dr Parviz Habibi.)
Sickle Cell Disease (SCD)

- Clinical Presentation
  - Usually diagnosed on neonatal screen
  - Manifestations of clinical symptoms can be as early as 6 months of age
  - Crisis
    - Splenic sequestration
    - Pain crisis
    - Aplastic crisis
      - Parvovirus B19 frequent cause of aplastic crises
Sickle Cell Disease (SCD)

• Clinical Presentation
  – Infections
    • Bacterial sepsis is the greatest cause of morbidity and mortality
    • Bacterial infection by encapsulated organisms is the most common at all ages
  – Functional asplenia as early as 6 months, by age 5 in most children
Sickle Cell Disease (SCD)

- Laboratory
  - Anemia
  - Sickle cells on smear
  - Target cells
  - Positive Sickle Prep.
    - Metabisulfite screen: Positive in both disease and trait
  - Hemoglobin electrophoresis
    - Disease: 90% HbS, 8% HbF, 2% HbA2, (No HbA)
    - Trait: 55% HbA, 43% HbS, 2% HbA2
Sickle Cell Disease

Peripheral smear (40x) from a patient with sickle cell disease showing sickle cells (black arrows), target cells (arrowhead), and a Howell-Joley body (red arrow)

*Pediatric Board Study Guide A Last Minute Review, Springer 2015*
Management

Prophylaxis –

Vaccines

susceptibility to infection because of functional asplenia, especially encapsulated organisms, e.g. *Streptococcus pneumoniae* and *Haemophilus influenzae* type B, meningococcus

Penicillin

To ensure full coverage of all pneumococcal subgroups, **daily oral penicillin throughout childhood** should be given.

Folic acid

Patients should receive once-daily

Vasoocclusive crises should be minimised by avoiding exposure to cold, dehydration, excessive exercise, undue stress or hypoxia.
Treatment of acute crises – Painful crises

Analgesia according to need (may require opiates)

Good hydration (oral or intravenous as required);

*infection* should be treated with antibiotics;

*oxygen* if the oxygen saturation is reduced.

*Exchange transfusion* for acute chest syndrome, stroke and *priapism.*
Treatment of chronic problems – Hydroxyurea

Crecurrent hospital admissions for painful vaso-occlusive crises or acute chest syndromemay benefit from hydroxyurea, a drug which increases their HbF production and helps protect against further crises. It requires monitoring for side-effects, especially white blood cell suppression.

MBT

The most severely affected children (1–5%) who have had a stroke or who do not respond to hydroxyurea may be offered a bone marrow transplant. This is the only cure for sickle cell disease but can only be safely carried out if the child has an HLA-identical sibling who can donate their bone marrow – the cure rate is 90% but there is a 5% risk of fatal transplant-related complications.