Sickle cell disease

- HbS → >70% of Hb in RBCs
  no HbA.
- HbS → protective against falciparum malaria
- HbF – 10-30%
- no HbA.

⇒ Hemoglobinopathies characterized by qualitative defect in Hb synthesis.

Sickle cell anemia ($\beta^S\beta^S$)	Sickle cell trait ($\beta\beta^S$)
• homozygous state.	• heterozygous state.
↓	↓
both β globin chains are abnormal.	one gene is defective.
	other gene is normal.

→ Sickle cell anemia is an autosomal recessive disorder with Extravascular hemolysis.

→ Sickle cell anemia is homozygous state in which both β-globin chains are abnormal.

∈ Tio pathogenesis.

- there is production of abnormal Hb → called HbS. Sickle Hb.

↓ Due to.

- missense point mutation.

↓

Substitution of glutamic acid by valine in 6th position of β globin chain.

↓

alters stability / solubility of Hb. & produce hemolytic anemia.

Robbins: Sickle cell disease is a common hereditary hemoglobinopathy caused by point mutation in β globin that promotes polymerization of deoxygenated hemoglobin, leading to red cell distortion, hemolytic anemia, microvascular obstruction and ischemic tissue damage.

Molecular Basis of Sickling

- low O_2 tension.

↓

HbS molecules undergo aggregation & polymerization.

↓

If low O_2 tension continues

↓

aggregated HbS form long rod like fibres → Tactoids

↓

tactoids grows in length beyond d of RBC

↓

distort RBC shape - Sickle shape.

↓

predisposes to stasis & Vascular occlusion

↓

when O_2 tension return to normal

↓

Sickle red cell return to normal shape

↓

recurrent sickling → cell membrane damage & hemolysis

↓

Irreversibly Sickled cell

↓

repeated sickling → dehydration

↓

rigid & nondeformable RBC

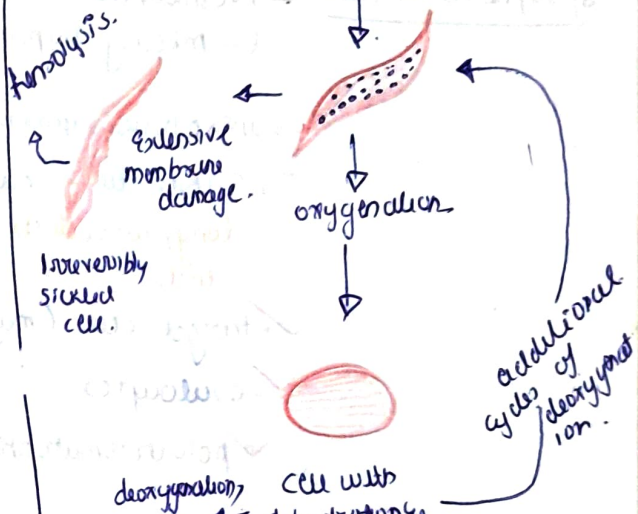
Pathogenesis of Intravascular Occlusion

HbS

↓

deoxygenation

↓



↓

microvascular occlusion.

Laboratory findings.

peripheral blood - Hb ↓.
PCV ↓
ESR ↓. (as sickle cell do not form Roulewx)
reticulocyte ↑ - 3-10%.

peripheral smear. - Normocytic normochromic to mildly hypochromic.

- ✓ anisopoikilocytosis.
- ✓ Sickle cell - characteristic. long, curved cell with pointed ends.
- ✓ target cells (may).
- ✓ ovalocytes.
- ✓ polychromatophilia.

WBC → mildly ↑ ; shifted left
platelets → mildly ↑

Bone marrow

- Cellularity → hypercellular.

Erythropoiesis: Compensatory normoblastic. → Extramedullary may. Erythroid hyperplasia.

↓

marrow expansion (cortex in severe case) roentgenograms.

myelopoiesis - Normal.
megakaryopoiesis - Normal.
Iron stores - increased.

Serum findings.

- Serum Bb → raised and predispose to pigment gall stones.
- Iron stain → ↑ Fe
  ferritin.
  transferrin
- serum haptoglobulin ↓.
- urine urobilinogen ↑

(1) Sickling Test – Diagnostic Test for sickle cell anemia.

- principle → sickling is induced
  ↓
  by adding 2% Sodium metabisulphite. (reducing (oxygen consuming) agent)
  or sodium dithionite. to blood sample.
  ↓
  Red cells with Hbs show
  Sickled and Holly leaf appearance.
  ↓
  Diagnostic of sickle cell anemia.

(2) Solubility Test

- add anticoagulated blood to reducing reagent solution → phosphate buffer.
  Saponin.
  Sodium dithionate.
- RBCs are hemolyzed.
- If Hbs is present → reduced by dithionate.
  ↓
  Tactoids
  ↓
  reflect light
  ↓
  TURBID

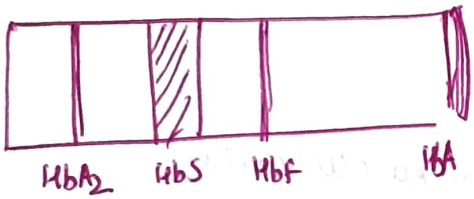
If.
- Hb - Normal
  ↓
  Clear solution

③ Hb Electrophoresis → Hbs slow moving.
Compared to HbA & HbF.

④ HbF Estimation → homozygous → 10-30% of Hb.

⑤ HPLC → used in confirmation of diagnosis.

High performance
liquid chromatography.



Clinical features.