SICKLE CELL ANEMIA:

→ Disease is a hemoglobinopathy that include (SS) & sickle cell trait (AS).
→ homozygous state in which both the β globin chains.

FEATURES:

caused by mutation in β globin that produce sickle hemoglobin (HbS)
→ HbS is more in their RBC than HbA.
↳ It is protective Against falciparum malaria.
→ Autosomal Recessive disorder

PATHOGENESIS

β chain mutation
↓
substitution of glutamic Acid by Valine in the 6th position of the β globin.
↓
Production of Abnormal sickle (HbS)
↓
Sickling during low O2 tension
↓
Reversible sickling
↓
Recurrent attack of sickling
↓
Formation of Irreversible sickle cells
↙ ↘
Microvascular occlusion by Irreversible sickle cells → ischemia pain crisis

Intravascular hemolysis of Irreversible sickled cells → Moderate severe hemolytic Anemia

MOLECULAR BASIS:

→ During low O2 tension → HbS molecules undergo aggregation & polymerization

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These aggregated HbS molecules form long needle-like fibres. (pseudocrystalline structure called tactoids) within RBC.

↓

These tactoid grows length beyond diameter of RBC & distort RBC shape.

↓

RBC become elongated, assumes a shape of sickle (holly leaf) cause stasis of vascular occlusion

Reversal of sickling → Initially Reversable when Oxygen Return to normal.

↓

sickling Returns to normal

↓

RBC membrane get destroyed during each episode of sickling → causes membrane skeleton

↓

Irreversibly sickled cells → hemolysis

with Recurrent sickling cause Abnormal shape Red cell membrane damage → RBC become more Rigid & Nondeformable

↓

susceptible to hemolysis

Factors favouring

Slowing of Blood stream

↑ MCHC

↓ PH

Temp Above 37°

PATHOLOGIC CONSEQUENCE OF SICKLING:

These Rigid sickle cell are destroyed in spleen.

↓ lead to

hemolytic Anemia.

Life span of RBC is reduced to 20 days

↑ unconjugated bilirubin & pigmented Gallstones.

Vascular obstruction:

These cells are Rigid & form Aggregates.
block small B.V. → produce Ischemic tissue damage & pain crisis.

→ Vascular congestion, thrombosis & infarction
mainly affect spleen, Bone Marrow → As B.F is slow.

→ sickle cell express higher level of Adhesion molecule & thus become Abnormally sticky to the endothelium.

Pain crisis: 4 types — Vaso occlusive, hemolytic, Aplastic → sequestration crisis

Vasocclusive → most common type produce → hypoxic, infarction.

Hemolytic crisis → ↑ in hemolysis

Aplastic → ↓ Red cell production. Accompanied by Reticulocytopenia

→ Sequestration crisis → sudden trapping of blood in the spleen, spleen or liver cause Rapid enlargement of these organs.

Clinical features:

symptom appear after 6 months of Age
↳ cause HbF is in the 1st 6 months of life has a protective Role

- severe infection.
→ Acute chest syndrome.
→ splenic sequestration, stroke.
→ impaired of growth in children.
→ chronic organ damage.

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Lab findings:

= ↓Hb, ↓PCV, ↓ESR → due to sickle cell Anemia cannot form Rouleaux

= ↑Reticulocyte count

Peripheral smear:

→ normocytic normochromic

– Anisopoikilocytosis – size & shape

→ long elongated boat shaped cells

→ Target cells → ovalocytes may also be seen

→ ↑Reticulocytes.

→ WBC ↑

→ Platelet ↑

BM

→ Hypercellular

→ Normoblastic erythroid hyperplasia

→ Iron stores ↑ed

→ Classical appearance in Radiograph → due formation of new bone

– Extramedullary hemotopoiesis

Tests

→ sickling test →

→ Hb electrophoresis.

→ Estimation of HbF

→ High performance liquid chromatography.