Sickle Cell Anemia

- RBC becomes crescent shaped or sickle shaped
- Gets destroyed easily and quickly causing Anemia.

- Sickle cell disease ⟶ caused by defective Hb

Hb ⟶ O_2 carrying Protein in RBC.
⟶ made up of 4 peptide chain bound to a heme group

Hb A made up of —

→ 2 α-globin [DEPTH OF BIOLOGY]
→ 2 B-globin Peptide chain

Hb A is the primary Hb gets affected in Sickle cell Anemia.

- The B-Globin chains ends up being malformed. This is because Mutation in B globin gene, or HB B gene.
- SCA is Autosomal Recessive Disease

→ So, mutation in both copies of beta globin gene is needed to get the disease.

→ In the case, if person has just one copy of the mutation and one normal HBB gene then they are Sickle cell carriers also called Sickle trait. [DEPTH OF BIOLOGY]

→ Having Sickle trait does not cause Health problem unless the person is exposed to extreme condition.
like — High altitude, Dehydration, where some sign and Symptoms of sickle cell disease can occur and pop up. [DEPTH OF BIOLOGY]

→ Malaria chances decreases ⟶ ∴ Sickle cell RBC (Africa)

In Africa Sickle trait are actually advantage called Heterozygote advantage.

[DEPTH OF BIOLOGY]

• SC mutation is a non-conservative missense mutation that happen in 6th Amino acid of Beta chain

Normal Condition: CTC GAG → glutamic (Hydrophillic)

Sickle cell anemia diseased Person: CAC GUG → valine (Hydrophobic)

It is an example of point Mutation

→ A Hb tetramer with 2α-globin and 2 mutated β-globin protein called sickle Hb or HbS → sickling process.

→ HbS ⟶ carry O_2 well

But when deoxygenated ⟶ HbS changes its shape.

→ This allows it to aggregate with other HbS protein and form long polymer that distort the RBC into Crescent shape or sickle shape — process called Sickling

Favourable condition for sickling ⟶ Includes acidosis ⟶ ↓se Hb affinity for O_2 and small low flow vessels where RBC Hb molecule have plenty of time to dump lots of O_2 molecule.

→ Repeated sickling of RBC ⟶ Damage their cell Membrane and promote premature destruction

[DEPTH OF BIOLOGY]

Since this happen within Vasculature

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It is called Intravascular Haemolysis

↓

This destruction of RBC just not lead to anemia (RBC↓ or Hb↓) but also means lots of Hb spilling out.

• +Hepatoglobin ⟶ & get Recycled

Free Hb in Plasma

Hepatoglobin used to clear free Hb.

[DEPTH OF BIOLOGY]

Low level of Hepatoglobin is a sign of Intravascular Haemolysis.

* Recycled of that Haeme group yeild

↓

unconjugated Bilirubin

[DEPTH OF BIOLOGY]

↓

its high conc. can cause.

Scleral Icterus, Jaundice and bilirubin Gall stones

→ To counteract the anemia and Sickle cell Disease

Bone Marrow makes increased no. of Reticulocytes (Immature RBC

This ends up & causing new bone formation

Expansion of Medullary cavities in skull.

and

Enlarged cheeks

Hair on end.

→ Extra Medullary Hematopoiesis. [DEPTH OF BIOLOGY]

Extra = outside; Medullary = Bone marrow; Hematopoiesis = RBC Production

In liver ⟶ cause Hepatomegaly

① In Sickel form, RBC tend to get stuck in capillaries called vasoocculusion

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starting In Infancy (childhood) ⟶ They can clog up blood flow in the bones of the hands and the feet causing dactylitis or swelling and pain in digits.

↓ [DEPTH OF BIOLOGY]

later they stuck in other bones and causing a sickle pain crisis or Avascular necrosis of the bone..

② # RBC also clog up in spleen.

↓

lead to Infract of the spleen

↓

overtime

↓

It leads to an auto splenectomy.

Having absent or Non functional spleen makes a person susceptible to encapsulated bacteria Like streptococcus Pneumonia, Homophilius Influenza and Salmonella species

③ → of Red blood cell can get stuck in the cerebral vasculature causing vessle damaged resulting in strokes. → excessive damage - Moya Moya dz.

④ → Also stuck in Blood vessle of lungs → leading to Acute chest Syndrome

⑤ → Clogging in Renal papillae can cause Necrosis

↓

Blood and Protein split out with urine.

⑥ → clogging in vasculature of Penis cause → Priapism (painful prolonged erection)

Diagnosis :-

- Newborn blood spot screen.
- Blood Smear → looking for sickle cell.
- By Identifying HbS using protein electrophoresis.

Treatment :-

① Hypoxia
Acidosis
Dehydration
} lead to RBC (Sickle shape

• Impersoned with oxygen and fluids.

(2) opiods ⟶ used to Mange Pain.

(3) Antibiotic ⟶ treat underlying bacterial Infection from acute chest Syndrome.

(4) Blood Transfusion

(5) Hydroxyurea ⟶ ↑se the amount of γ-Globin ⟶ results in more fetal Hb or (HBF) ⟶ Primary Hb at birth

(6) More Rarely
- ⟶ Bone Marrow Transplant
- ⟶ Gene Therapy