Sickle cell anemia :

Inherited blood disorder

RBC have abnormal shape like Sickle

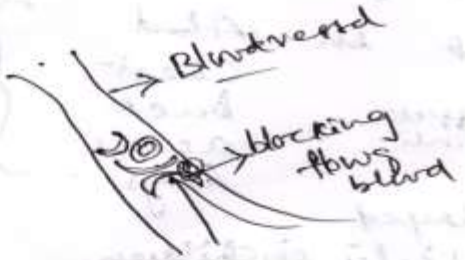
Bcoz of their shape — becomes rigid and sticky

↓

Prone to getting trapped in small vessels

↓

Blocks blood from reaching different part of body.



Hb will be defective type

↓

and

O_2 level of entire red cells get low

Defective Hb% forms long rods

Then long rods stretch the RBC into long abnormal Sickle shape

Normal life of RBC ——— ?

In contrast, Sickled blood cells last only 10 – 20 days.

Etiology Anemia is caused by ch. destruction of RBC

Symptoms: 1. Fatigue
2. Shortness of breath
3. Pale skin & finger Nails
4. Pain induced in Abd, Chest, back, arms, legs
5. Painful crisis can affect joints
6. Growth rate slow → delayed Puberty in children.

} Lack of O_2 can damage organs & limbs - Causes severe pain in affected area. Painful episodes called Sickle cell crisis.

Normally, Haemoglobin contains Iron moiety and 4 polypeptide chain

HbA: Adult: 2 α chains
2 β chains

Along with it (Small Amounts) } **HbA_2** → 2 α chains.
2 δ chains

And fetal Hb/ **HbF** → 2 α chains
2 γ chains

Sickle cell Anemia **HbS** Result: by point

Mutation in 6th position of β chain that leads to replacement of Glutamate residue to a Valine resulting sickle Hb — HbS

when it is obtained from Parents ~~HbA & HbS~~ determines the type of Adult Hb they will have.

Genes always come in pairs to children one from Mother & one from father

∴ Every Individual inherits 2 Adult Hb genes.

(HbA)

Normal Hb from their parents Ex: ~~Hb~~

Ex Sickle cell Hb (S) (HbS)

Sickle cell traict : when a person acquires HbA from one parent

& Sickle cell Hb 'S' from other

↓

They have Sickle cell trait

(4)

written as HbAS → considered as Healthy Carrier.

↓

Does not have an illness without any symptoms

⊕

If a couple are both carriers (traits of Sickle cell)

have a chance of their child can inherit sickle cell disease.

(Hb SS)

(5) Pathogenesis :

Hbs Molecules undergo polymerization when 'Deoxygenated'

Red cell cytosol which is freely flowing liquid

↓ becomes

Viscous gel as Hbs aggregates form

↓

With continued deoxygenation aggregated Hbs Molecules assemble into long needle like fibers in red cells producing Distorted sickle Shape

Presence of Hbs causes pathologic manifestations

1. Ch. Hemolysis
2. Microvascular occlusions.
3. Tissue damage.

O_2

↓

Deoxygenation

↓

Polymerization of Hb

↓

Sickling of red cells.

↓

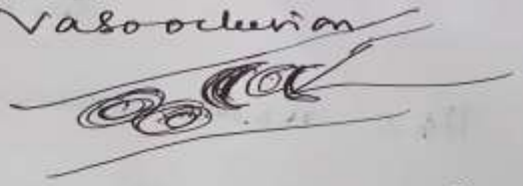
Endothelial damage

↓

RBC & Leukocyte adherence to Endothelium

↓

Vaso occlusion



Due to Deformed Shape HbS induces RBC Membrane damage

↓

Leading to Ca influx into the cell.

↓

Leads to Crosslinking of Membrane protein and activates the channels that allow efflux

of potassium and water from the cell

↓

Leads to RBC Dehydration Exacerbating sickling.

Vasoocclusive crisis results leading to Ischemia, Pain & Necrosis.

Further Hb is released from Haemolysed cells depletes NO (which is vasodilator)

↓ leading

Vascular Smooth Muscle contraction (vasoconstriction)

&

Enhanced platelet aggregation

Occlusion further leads to Hypoxia of tissue.

&

Sets up condition for vicious cycle in which further sickling & Hypoxia occurs.

(8)

Treatment : 1. Rehydration ⊂ IV fluids helps RBC to relain Normal shape

As RBC More Likely to deform and assume Sickle shape if the condition of dehydration.

2. Blood transfusion : Packed cells to give.

3. Treatment ⊂ Drugs like Antibiotics — As infection may cause

Pain relieving — Codeine

NSAID's