

# Thalassemia

Genetic Disorder

[DEPTH OF BIOLOGY]



Deficiency in the production of  $\alpha$ -globin chains of Hb which is the O<sub>2</sub> carrying protein in RBC.

- \* Normally, Hb is made up of 4 globin chains each bound to a haeme group.

→ There are 4 major types of Globin chains

( $\alpha, \beta, \gamma, \delta$ )

These combine in diff. ways to give rise to diff. Hbs.

- Hb-F (F = fetal Hb) → 2 $\alpha$  globin and 2 $\gamma$  globin chains
- Hb-A (major form of adult Hb) → 2 $\alpha$  globin, 2 $\beta$  globin
- HbA<sub>2</sub> (amounts for small fraction of adult Hb in blood). made up of → 2 $\alpha$  globin and 2 $\delta$  globin chains

- \*  $\alpha$  chain synthesis is controlled by 4  $\alpha$  genes [DEPTH OF BIOLOGY]



Two on each copy of chromosome 16

#  $\alpha$ -Thalassemia → caused by mutation in  $\alpha$ -genes  
most commonly gene deletions

- Mutations are inherited in Autosomal Recessive pattern (for disease to occur → both paired gene need to be mutated).

→ If a person have one defected  $\alpha$ -gene (called silent carrier) [DEPTH OF BIOLOGY]

∴ they don't have symptoms but can pass the disease to their offspring.

# If the person has 2 defected  $\alpha$ -genes the person has  $\alpha$ -Thalassemia minor → cause mild symptoms.

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This can either be caused by Cis deletion where the mutated genes are on same chromosome or a

Trans deletion → the mutated genes are on 2 diff. chromosomes. [DEPTH OF BIOLOGY]

- \* Cis deletion variant → more prevalent in Asians
- \* Trans deletion variant → more prevalent in Africans

# If there are 3 defective  $\alpha$ -genes

HbE disease



called HbH or HbH disease this is caused by excess  $\beta$  chain, which clump together within developing R.B.C to form tetramers or beta<sub>4</sub> and give rise to form of Hb called HbH or Hbh.

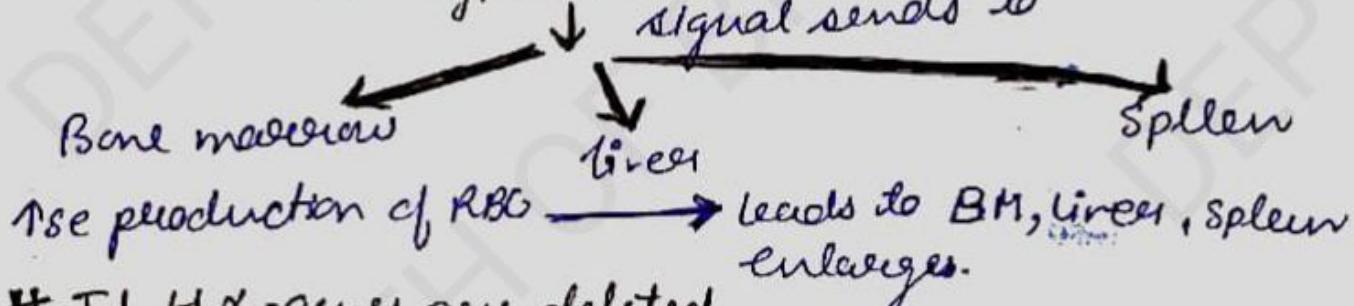
\* Hbh molecule can cause hypoxia in 2 diff. ways-

1. Damage RBC Membrane

results in intramedullary hemolysis (when RBC are destroyed by macrophages in the spleen).

2. Hbh has very high affinity for O<sub>2</sub> & does not release O<sub>2</sub> to tissues.

In hypoxic condition [DEPTH OF BIOLOGY]



# If 4  $\alpha$ -genes are deleted

results in Hb Bart's Hydrops fetalis.

(problem faced during foetal life.)

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where Gamma chains form tetramers (in the absence of  $\alpha$  chains called Hb Bart's gamma 4)

It has super-deep affinity for  $O_2$  about 100 times more than the normal Hbs

Tissue don't get  $O_2$  → Severe Hypoxia.  
results in ↓

- \* Edema all over the body called hydrops foetalis
- \* High cardiac output failure.
- \* massive hepatosplenomegaly

### Symptoms

- Pallor
- shortness of breath
- Easy fatigability
- skeletal deformities.
- Hepatosplenomegaly.

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### Diagnosis

1. Blood test → Hb↓  
↓ ↓ MCH (Mean Corpuscle Hb)  
↓ ↓ MCV (Mean Corpuscular Vol.)
2. Hb Electrophoresis
3. Confirmed Genetic testing [DEPTH OF BIOLOGY]
4. Blood smear → Microcytic (small)  
↓ ↓ Hypochromic (pale)
5. In Moderate Thalassemia → Ball like RBC → due to Pkt. of Hb<sub>w</sub> molecule.

### Treatment

- Patient with mild Thalassemia → don't need treatment.
- Severe Thalassemia
  - (1) → Blood Transfusion
  - (2) → Hb Bart's hydrops foetalis →
    - Intrauterine transfusion
    - Bone Marrow Transplantation

[DEPTH OF BIOLOGY]