Thalassemia

[DEPTH OF BIOLOGY]

Genetic Disorder

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Deficiency in the production of α-globin chains of Hb which is the O_2 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

(α, β, γ, δ)

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

- Hb-F (F = fetal Hb) ⟶ 2α globin and 2γ globin chains.
- Hb-A (major form of adult Hb) ⟶ 2α globin, 2β globin
- HbA_2 (amounts for small fraction of adult Hb in blood). made up of ⟶ 2α globin and 2δ globin chains

* α chain synthesis is controlled by 4 α genes [DEPTH OF BIOLOGY]

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Two on each copy of Chromosome 16

α-Thalassemia ⟶ caused by mutation in α-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 α-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 α-genes the person has α-Thalassemia minor ⟶ cause mild symptoms.

[DEPTH OF BIOLOGY]

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 α-genes

Moderate disease

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called HbH or Hbh disease this is caused by excess β chain, which clump together within developing R.B.C to form tetrameers or beta 4 and give rise to form of Hb called HbH or Hbh.

Hbh molecule can cause Hypoxia in 2 diff. ways—

1. Damage RBC Membrane

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results in intramedullary Hemolysis (when RBC are destroyed by Macrophages in the spleen.

2. HbH has very high affinity for O_2 & does not release O_2 for tissues.

In hypoxia condition [DEPTH OF BIOLOGY]

↓ signal sends to

Bone marrow ← Liver → Spleen

↑se production of RBC → leads to BM, Liver, Spleen enlarges.

If 4 α-genes are deleted

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results in Hb Barts Hydrops fetalis.

(problem form during fetal life.)

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where Gamma chains form tetrameres (in the absence of α chains called Hb Bart's gamma 4

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It has super-duper affinity for O_2 about 100 times more the normal Hb

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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 → ↓Hbv, ↓se MCH (Mean Corpuscle Hb), ↓se MCV (Mean Corpuscular Val.)
2. Hb Electrophoresis
3. Confirmed Genetic testing
4. Blood smear → Microcytic (small), Hypochromic (pale)
5. In Moderate Thalassemia → Ball like RBC → due to ppt. of Hbv molecule.

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Treatment

- Patient with mild Thalassemia → don't need treatment.
- Severe Thalassemia

① → Blood Transfusion

② → Hb Bart's hydrops fetalis → Intrauterine transfusion, Bone Marrow Transplantation

[DEPTH OF BIOLOGY]