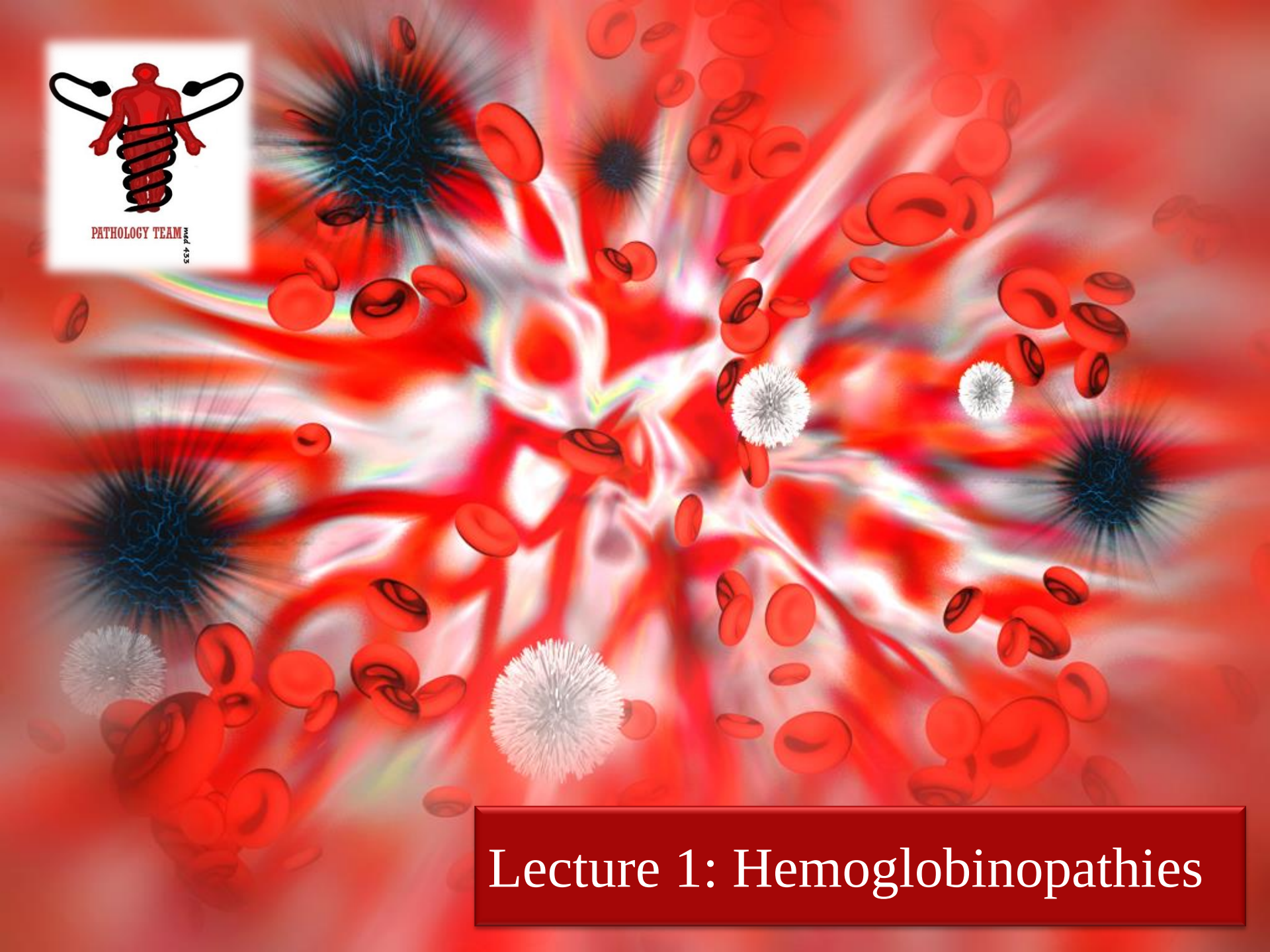


Lecture 1: Hemoglobinopathies

Objectives

- List the types of hemoglobinopathies and the definition of each.
- Introduction about RBCs formation.
- Brief talking about Hemoglobin types.
- Brief talking about the structure and synthesis of Hemoglobin.
- Thalassemia
- Epidemiology of Thalassemia.
- Alpha and Beta Thalassemia and their classification.
- The clinical manifestation of Thalassemia.
- Diagnosis.

Symbols :
α = alpha
β = beta
ε = epsilon
ζ = zeta
γ = gamma
δ = delta

If you would love to read about alpha thalassemia in arabic
http://www.thalassaemia.org.au/resources/factshets2/arabic/alpha%20thal%20arabic.pdf

RBCs formation (hematopoiesis) and Age-dependent globins

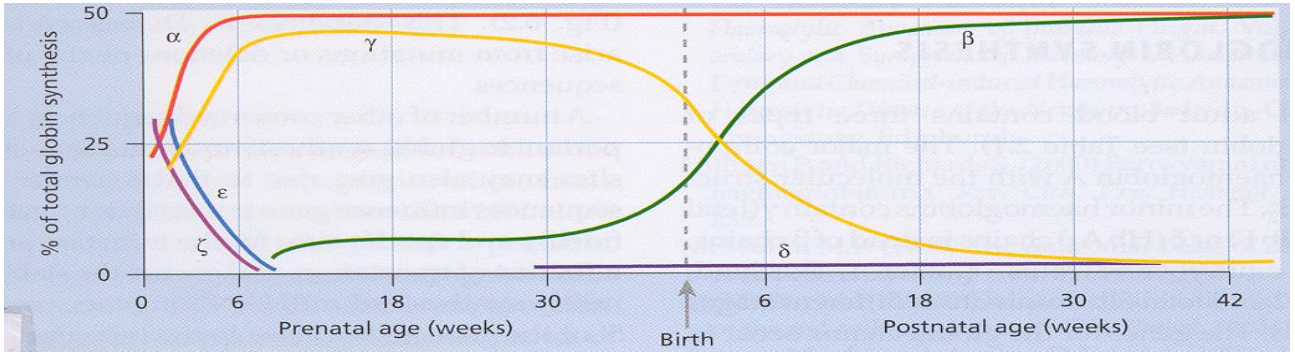
- **hematopoiesis:** RBCs are formed in different organs depending on the stage of life.

Time	Sites
Up to 2 months before birth	yolk sac
2- 3months before birth	liver , spleen
After birth	bone marrow *

- Bone marrow sites from most to least(vertebrae → sternum → pelvic bone → ribs → femur → tibia)

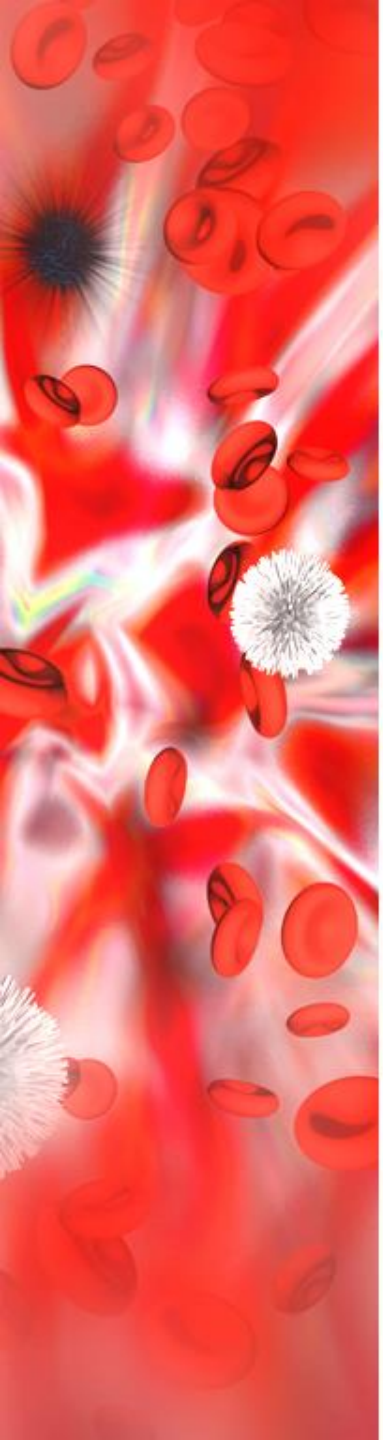
- Globin chains :

Prenatal	**(α - γ high amount)-(ζ- ε – β low amount)**
Postnatal	**α (remain) – β (increase) – γ (decrease) - δ**



Genes expressing of globin chains :

No. of chromosome	Globin chains
chromosome 16	α 1, α2, ζ
chromosome 11	(rest) β , ε , Aγ , Gγ ,δ



Types of Hemoglobins:

- Normal :

Stages	Types	Globin chains	Availability(in K.S.A)
Embryo	Gower1 Hb	2 ζ – 2 ε	
	Gower2 HB	2 α - 2ε	
	Portland Hb	2 ζ – 2 γ	
Fetus	HbF	2 α - 2γ	
Adult	HbA	2α – 2 β	95.0%
	HbA2	2 α – 2 δ	3.5%
	HbF	2 α - 2γ	1.5%

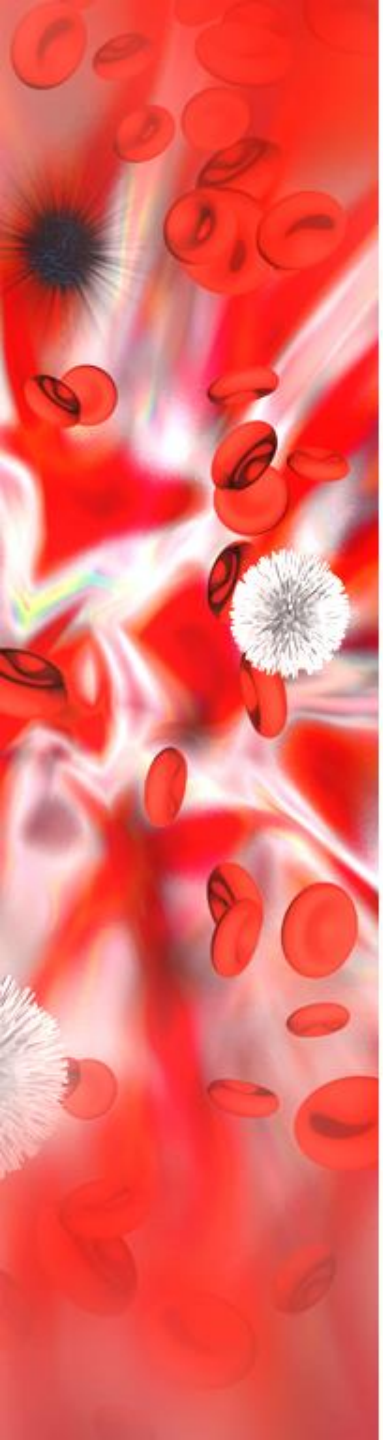
- You can observe that Alpha is present in most of the types of Hemoglobin.That's why it's expressed by 4 genes (2 in each chromosome).
- α globin consists of 141 Amino acids, while β has 146 Amino acids.

- Abnormal :

Name	Globin chains	
Hb H	-	4 β
Hb Bart's*	-	4γ
Hb Lepore	rare 2 (δβ) 2α (not important)	

Notes:

- HbH and Hb bart's is considered as α-Thalassemia because of the absence of α globins.
- Hb bart's found normally at birth but shouldn't exceed 0.5%



Types of Hemoglobinopathies

- Hemoglobinopathies are sub classified according to the structure and function of hemoglobin into :

❖ Thalassemia: an inherited autosomal recessive disorder in which the protein part (Globin) of the hemoglobin is completely or partially missed, resulting in inability of the formed Hemoglobin to carry Oxygen and Carbon dioxide to and from the lung.

❖ Abnormal Hemoglobins: a condition characterized by abnormal hemoglobin structure, due to an error in the sequence of amino acids which form the globin.

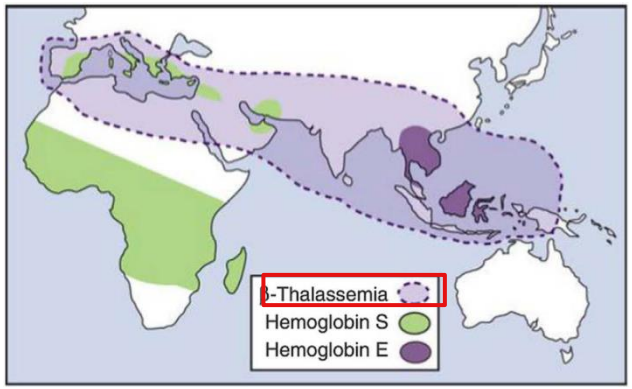
Examples: Sickle cell anemia , Hemoglobin C , Hemoglobin D…etc.

Thalassemia

can be Homozygous involving the pair of chromosomes or Heterozygous involving one chromosome .

- Epidemiology:

It's common in Arab peninsula, Mediterranean countries, India and Pakistan, South east Asia and saudi arabia.



- Types of Thalassemia :

❖ α-Thalassemia:

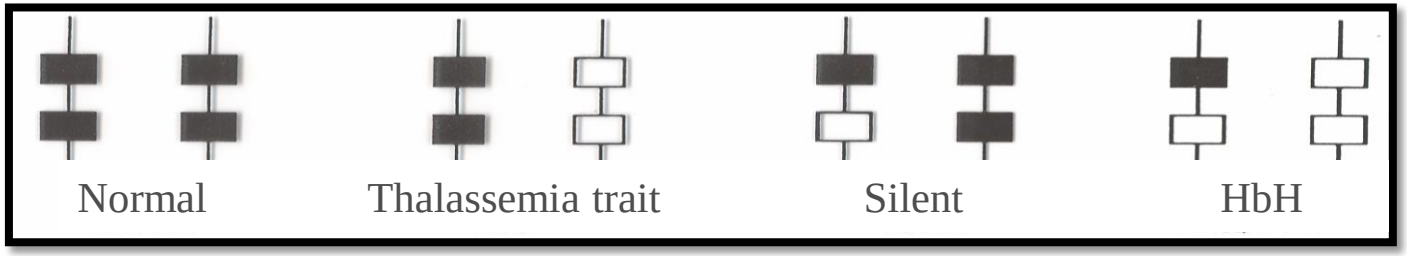
A condition in which α globin is partially or completely absent due to missed genes, which are responsible to express it.

Type	Description
Silent (carrier)	Missing one gene in one of the chromosome pairs (Heterozygous),usually no presenting symptoms.
Thalassemia trait	- Missing two genes, either in the same chromosome (Asian type) - one on each chromosome (African type).
HbH (moderate)	3 genes are missed. Only one gene remains.
Hydrops fetalis	All 4 genes are missed, the fetus cannot live without intervention.

Trait = mild

Thalassemia (Cont.)

When a man whit silent alpha-Thalassemia get married with a trait Asian alpha-Thalassemia woman, Their children's probabilities can be show below:



❖ β-Thalassemia:

A condition in which β globin is partially or completely absent due to missed genes, which are responsible to express it.

Classification can be done by 2 ways:

- According to Molecular factors such as: Synthesis of Beta globin, Beta mRNA activity, Beta gene presence and so on) into:

1/Beta+: the synthesis of Beta globin is partially decreased.

2/Beta0: the synthesis of Beta globin is completely lost.

The gene expressing Beta in both types could be present (Ferrara) or partially decreased (Indian).

3/δβ-Thalassemia*

4/Hereditary Prominent Fetal Hb (HPFH)*: HbF is the prominent type here (not HbA)

*In both types, the gene is deleted and the synthesis is completely lost.

Thalassemia (Cont.)

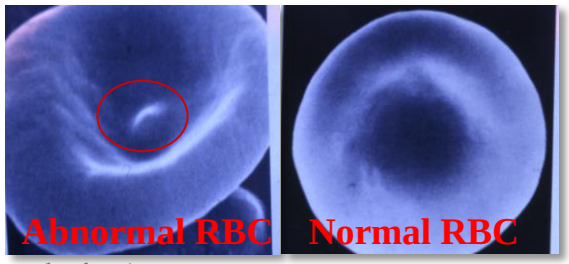
- **According to the concentration of Hb into**:

Type	Hb Conc.
Major	Less than 7g/dl
Intermedia	7-10g/dl
Minor	More than 10g/dl
Minima	Normal

The presenting symptoms are most severe in (Major) and least severe in minima.
There are some additional differences between these types (Please refer to the main lecture).

- Hematologic Features of the β-Thalassemia Syndrome

- **Hypochromia**
- **Microcytosis (all types except minima)**
- **Target cells** see pic
- Basophilic stippling
- Reticulocytes
- **Nucleated red cells** (normally shouldn't appear in circulation)



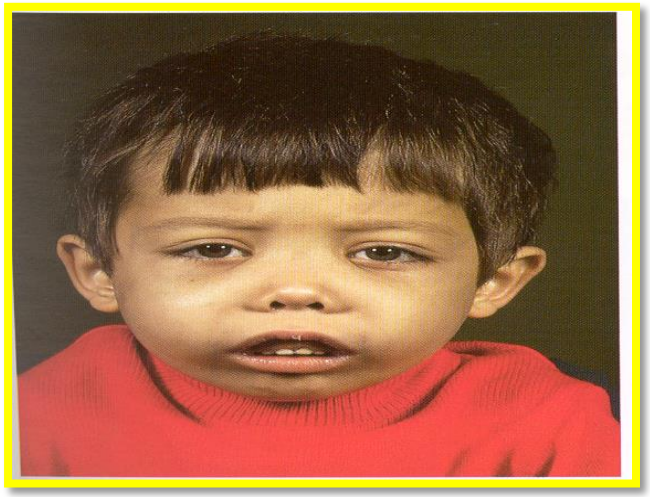
Notes

- A decrease in HbA2, indicates a benign form of α-Thalassemia.
- While an increase in the percentage of HbA2 is an indicator of β-Thalassemia

Clinical Manifestations of Thalassemia

- Pallor due to anemia
- Jaundice due to hemolysis
- Apathy and Anorexia
- Failure to Thrive فشل التطور و النمو
- **Hepato-splenomegaly**
- Skeletal Deformity (Under X-ray hair on end appearance*)
- Iron Overload due to RBCs breaking down

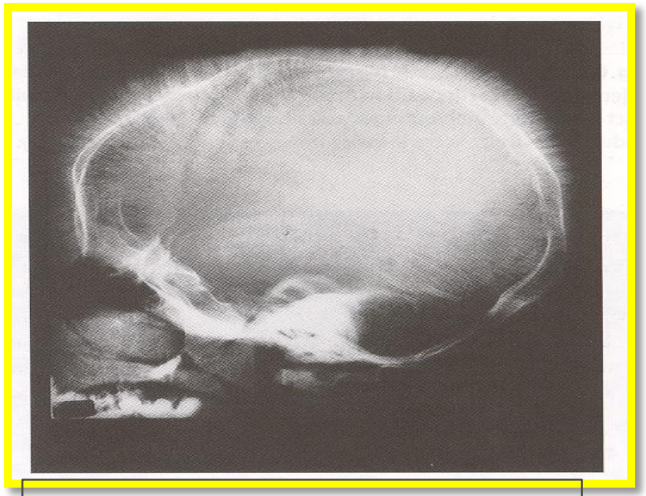
*Differential diagnosis of thalassemia and **only appears in major type**



In this photo, the Nose depression, Boozing forehead, maxillary prominence are observable.

MANAGEMENT OF THE THALASSEMIAS

- **Blood Transfusion**
- **Iron chelation therapy عملية ازالة (للمعادن تستخدم)**
- **Splenectomy**
- **Hormone replacement**
- **Bone marrow transplantation**
- **Gene therapy**



This X-ray picture is showing the hair-like projection (as a result of skeletal deformity) very clearly.

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Good luck …