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KING SAUD UNIVERSITY
COLLEGE OF MEDICINE
HAEMATOLOGY TEAM
GIT BLOCK

Haematology Block

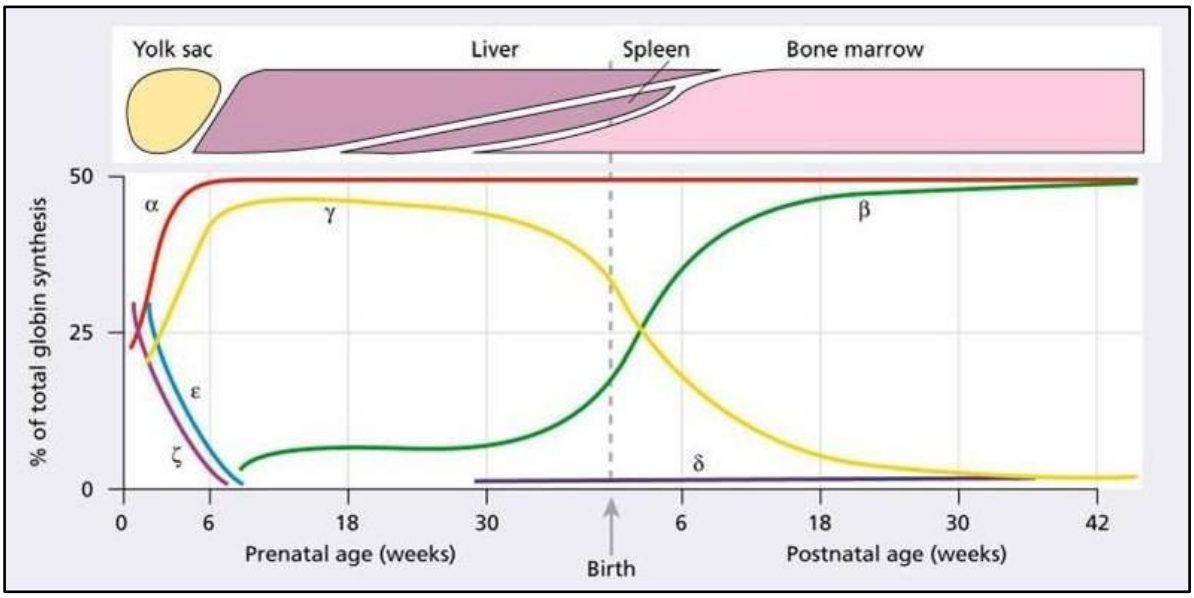
Lecture 1

Normal Haemoglobin

Nora AlRajhi

❖ Production and Formation of Red Blood Cells and Haemoglobin :

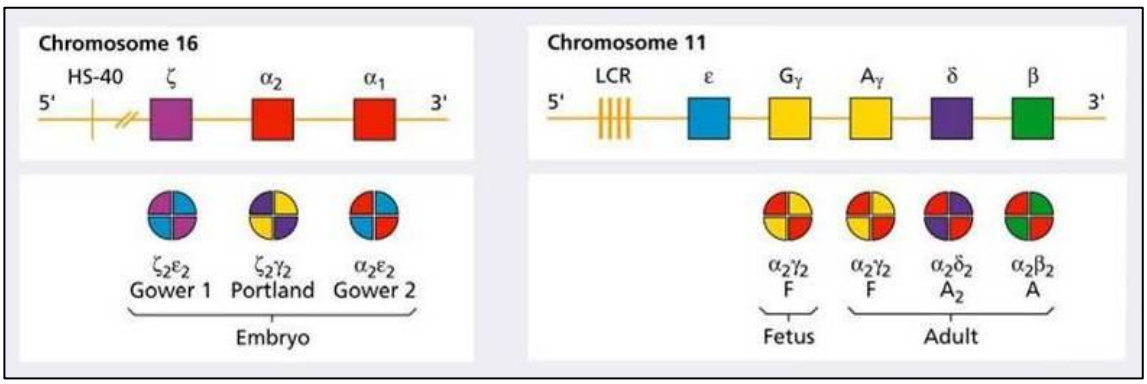
- The haematopoiesis of a human being starts in the **yolk sac,** and then the **liver** (main organ) takes over during the embryonic life.
- The **spleen** has a very slight role during the embryonic life.
- The **bone marrow** starts about 4 months of gestation and then it will be the main organ for haematopoiesis at birth.
- Best bones for producing blood are: Vertebrae, sternum, pelvic bones (ilium), and ribs.

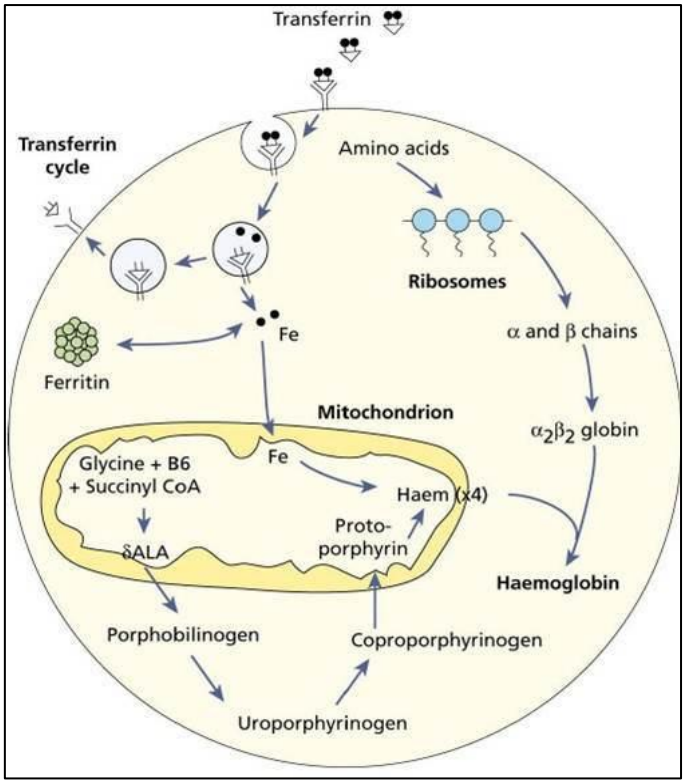


❖ Hemoglobin Synthesis :

- There are six types of genes which control the synthesis of globin chain.
- A haemoglobin molecule has 4 globin chains; each one is attached to haeme.
- These genes are found in two chromosomes: chromosome 11 and chromosome 16.
- **Chromosome 16:** There is Alpha (α) and Zeta (ζ) genes**.**
- **Chromosome 11:** There is Beta (β), Delta (δ), Gamma (γ), and Epsilon (ε).
- **Epsilon (ε)** and **Zeta (ζ):** Are genes that encode embryonic globin chains.
- **Alpha (α):** Stays throughout life.
- **Beta (β):** Appears in fetal life and continues throughout life.
- **Gamma (γ):** Through fetal life, continues throughout life but low.
- **Delta (δ):** Appears in 8 month fetus, continues throughout life but low.

Haemoglobin matures at one year of age





❖ Haeme :

One molecule of transferrin carries two atoms of iron.

- Occurs largely in the mitochondria.
- In serum, iron is carried to the cell by Transferrin.
- When the iron enters the mitochondria, it will combine to Protoporphyrin and form the Haeme.
- **Protoporphyrin** is formed by:
  - Glycine + B6 + Succinyl CoA under the action of the key rate limiting enzyme δ-aminolaevulinic acid (δALA) synthase will form Porphobilinogen outside the mitochondria.
  - Porphobilinogen will be converted later to Coproporphyrinogen.
  - After that, Coproporphyrinogen enters the mitochondria again and is converted to Protoporphyrin that will combine to iron to form Haeme.

❖ Globin :

- Amino acids are joined by ribosomes and make alpha (α) and beta (β) chains.
- 2 alpha (α_2) and 2 beta (β_2) chains are joined to make the globin.
- The haeme and globin fuse together and make haemoglobin.

Alpha (α) chains are made of **141** amino acids

Beta (β) chains are made of **146** amino acids

❖ Normal Haemoglobin :

Know the composition and percentage of the red ones!

NAME	Chains	
Haemoglobin A	α2	β2
Haemoglobin A2	α2	δ2
Haemoglobin F	α2	γ2
Haemoglobin H	-	β4
Haemoglobin Bart's	-	γ4
Haemoglobin Gower I	ζ2	Є2
Haemoglobin Gower II	α2	Є2
Haemoglobin portland	ζ2	γ2
Haemoglobin Lepore	α2	(δβ)2

EMBRYONIC (Up to 8 Weeks gestation)	**$\zeta_2 \epsilon_2$ Hb Gower I** **$\zeta_2 \gamma_2$ Hb Portland** **$\alpha_2 \epsilon_2$ Hb Gower II**		
FETAL	**$\alpha_2 \gamma_2$ HbF 60 - 85%** **$\alpha_2\beta_2$ HbA 15 – 40 %**		
ADULT	**HB**	**Caucasian**	**Saudi**
	$\alpha_2 \beta_2$ HbA	**97.0%**	**95.0%**
	$\alpha_2\delta_2$ HbA_2	**2.5%**	**3.5%**
	$\alpha_2 \gamma_2$ HbF	**0.5%**	**1.5%**

❖ Haemoglobins Present at Birth :

The maximum level of **A2** is 10%

Name	Percentage %
HbA	**15 – 40 %**
HbA_2	**< 0.3 %**
Hb F	**60 – 85 %**
Hb Bart's	**< 0.5**

- Hb A, Hb A2 and Hb F are normal and are present in adults.
- There is only one kind of fetal haemoglobin; Hb F.
- There are 3 kinds of embryonic haemoglobin; Gower I, Grower II, and Portland.
- Hb H is found in Haemoglobin H Disease (α-Thalassemia).
- Hb Bart's is found Hydrops Fetalis (α-Thalassemia).

Hb F has high affinity to oxygen and for that; the release of oxygen will be slowly, depending on the demand.

Summary

- **Embryo:** Yolk Sac.
- **Fetus (2 months):** Liver (main organ) and Spleen.
- **Fetus (4 months):** Bone Marrow.
- **At birth:** Bone Marrow (main organ).
- **Child:** Tibia and Femur.
- **Adult (30s-40s):** Vertebrae, Sternum, ilium and Ribs.
- There are six types of genes which control the synthesis of globin chain.
- Haemoglobin molecule has 4 globin chains; **Alpha (α), Beta (β)**, **Gamma (γ), Delta (δ)**, **Epsilon (ε)** & **Zeta (ζ).**
- **Chromosome 16:** Alpha (α) and Zeta (ζ) genes.
- **Chromosome 11:** Beta (β), Delta (δ), Gamma (γ), and Epsilon (ε).
- Haeme synthesis Occurs largely in the mitochondria.
- Iron enters the mitochondria; it will combine to **Protoporphyrin** and form the Haeme.
- Amino acids are joined by **ribosomes** and make Alpha (α) and Beta (β) chains.
- 2 Alpha (α_2) and 2 Beta (β_2) chains are joined to make the globin.
- **Hb A;** ($\alpha_2\ \beta_2$), **Hb A2;** ($\alpha_2\ \delta_2$)**, Hb F;** ($\alpha_2\ \gamma_2$)**, Hb H;** (β_4)**, Hb Bart's;** (γ_4)
- Hb A, Hb A2 and Hb F are normal and are present in adults.
- There is only one kind of fetal haemoglobin; Hb F.
- Hb A2 normal consumption; 3.5%.

EMBRYONIC (Up to 8 Weeks gestation)	**$\zeta_2\ \epsilon_2$ Hb Gower I** **$\zeta_2\ \gamma_2$ Hb Portland** **$\alpha_2\ \epsilon_2$ Hb Gower II**		
FETAL	**$\alpha_2\ \gamma_2$ HbF 60 - 85%** **$\alpha_2\beta_2$ HbA 15 – 40 %**		
ADULT	**HB**	**Caucasian**	**Saudi**
	$\alpha_2\ \beta_2$ HbA	**97.0%**	**95.0%**
	$\alpha_2\delta_2$ HbA_2	**2.5%**	**3.5%**
	$\alpha_2\ \gamma_2$ HbF	**0.5%**	**1.5%**