Structure and function of Haemoglobin

Introduction

- The main function of red blood cell
  - Transfer of O_2 from lungs to tissue
  - Transfer of CO_2 from tissue to lungs
- To accomplish this function red cells has haemoglobin (Hb)
- Each red cell has 640 million molecules of Hb

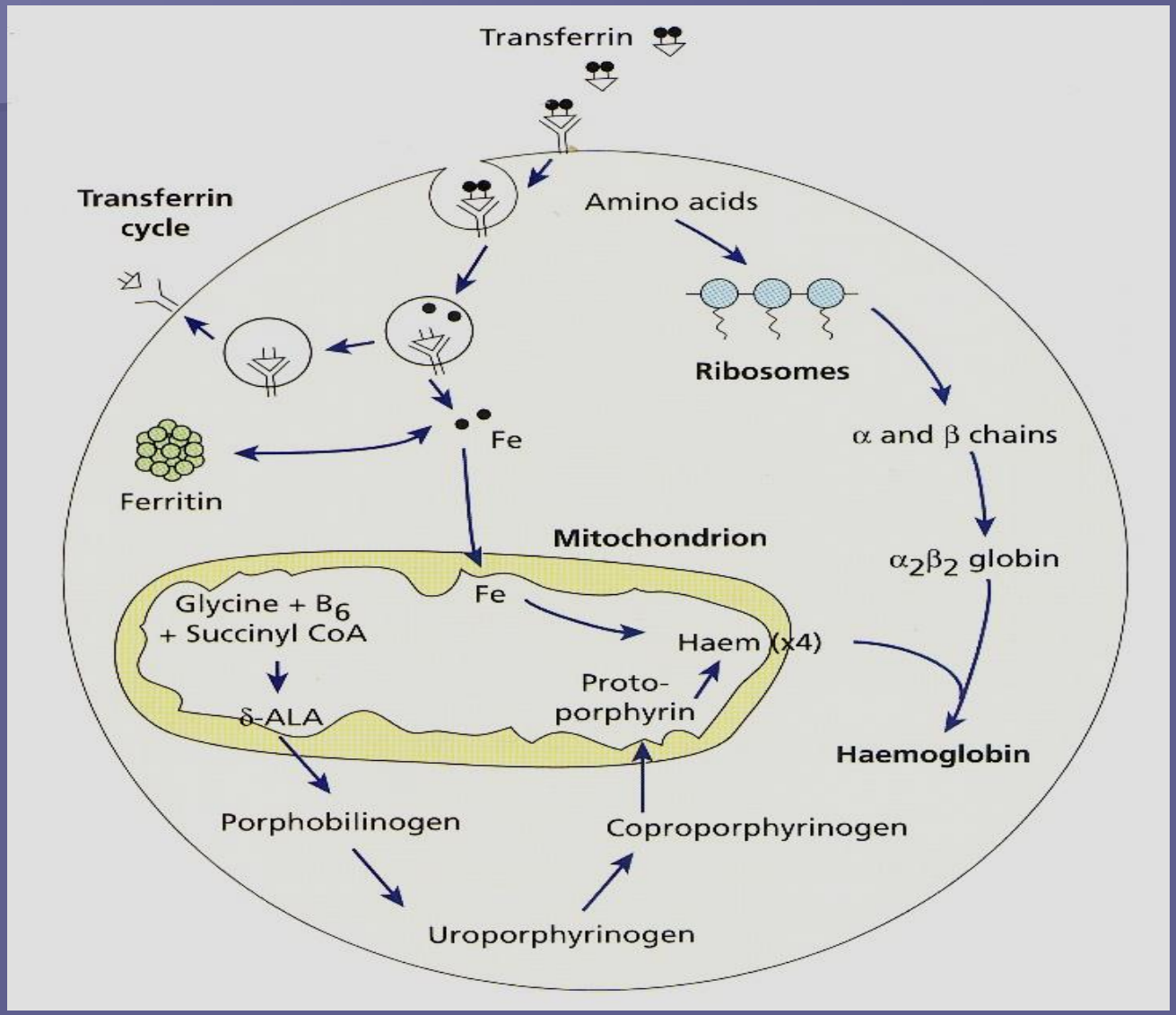
Introduction

- Haemoglobin (Hb), protein constituting 1/3 of the red blood cells
- Synthesis begins in proerythroblast
  - 65% at erythroblast stage
  - 35% at reticulocyte stage
- Two parts
  - Haem
  - Globin

Synthesis of Haemoglobin (Hb)

- Haem & globin produced at two different sites in the cells
  - Haem in mitochondria
  - Globin in polyribosomes
- Well synchronized

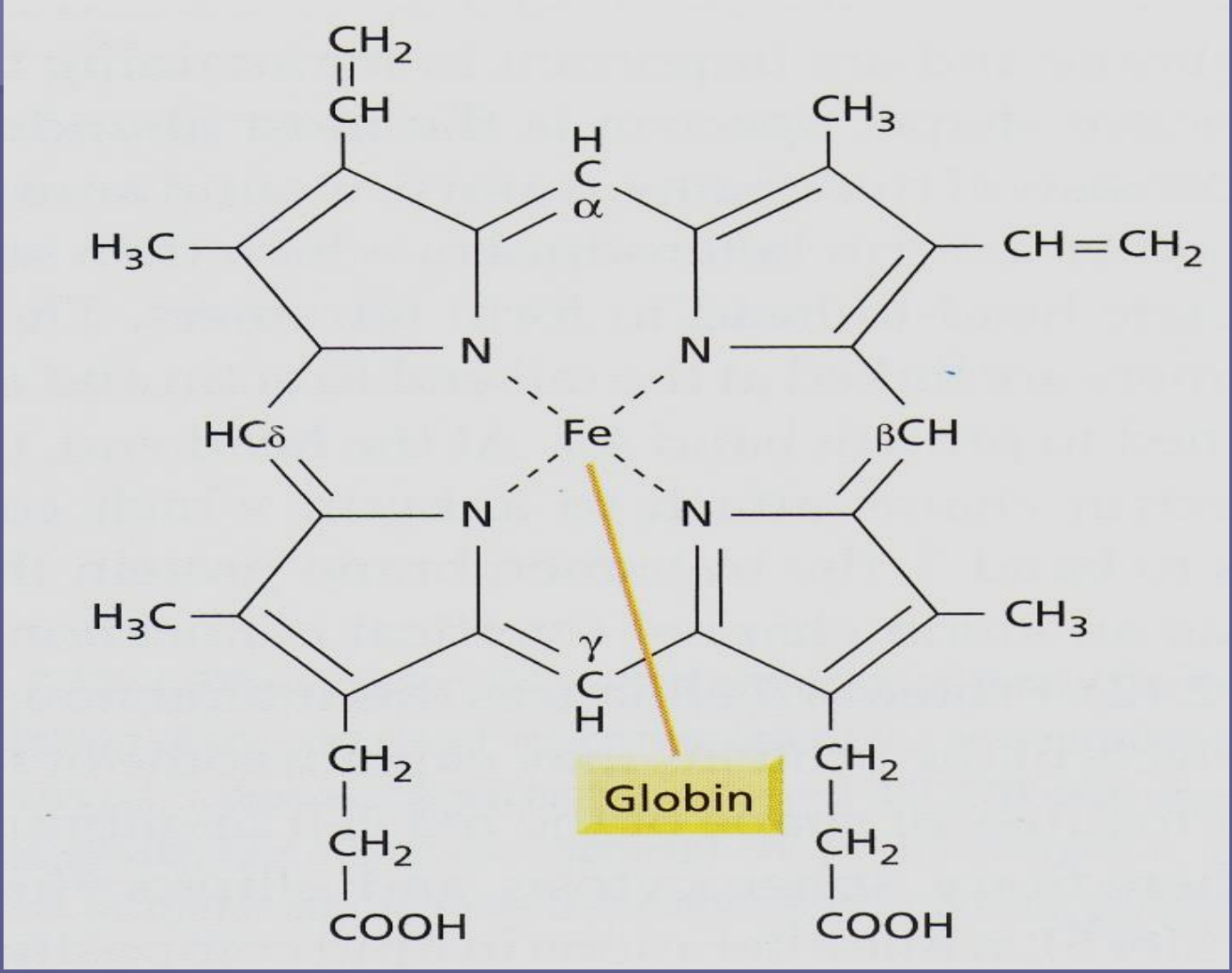
Synthesis of Haemoglobin



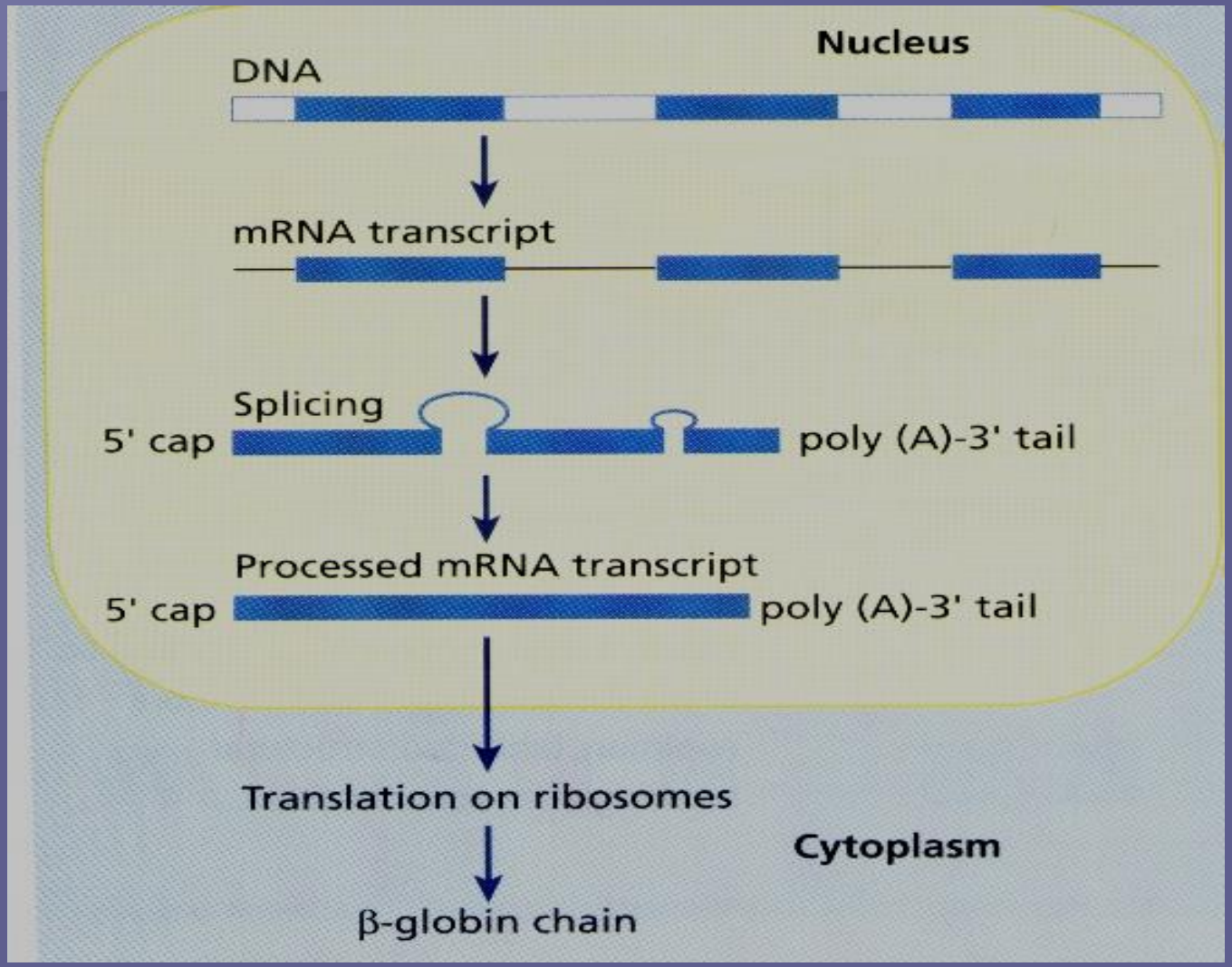
Synthesis of Haem

- Protoporphyrin ring with an iron atom in centre
- The main site is mitochondria as it contains ALAS
- Mature red cell does not contain mitochondria

Structure of Haem



Synthesis of globin

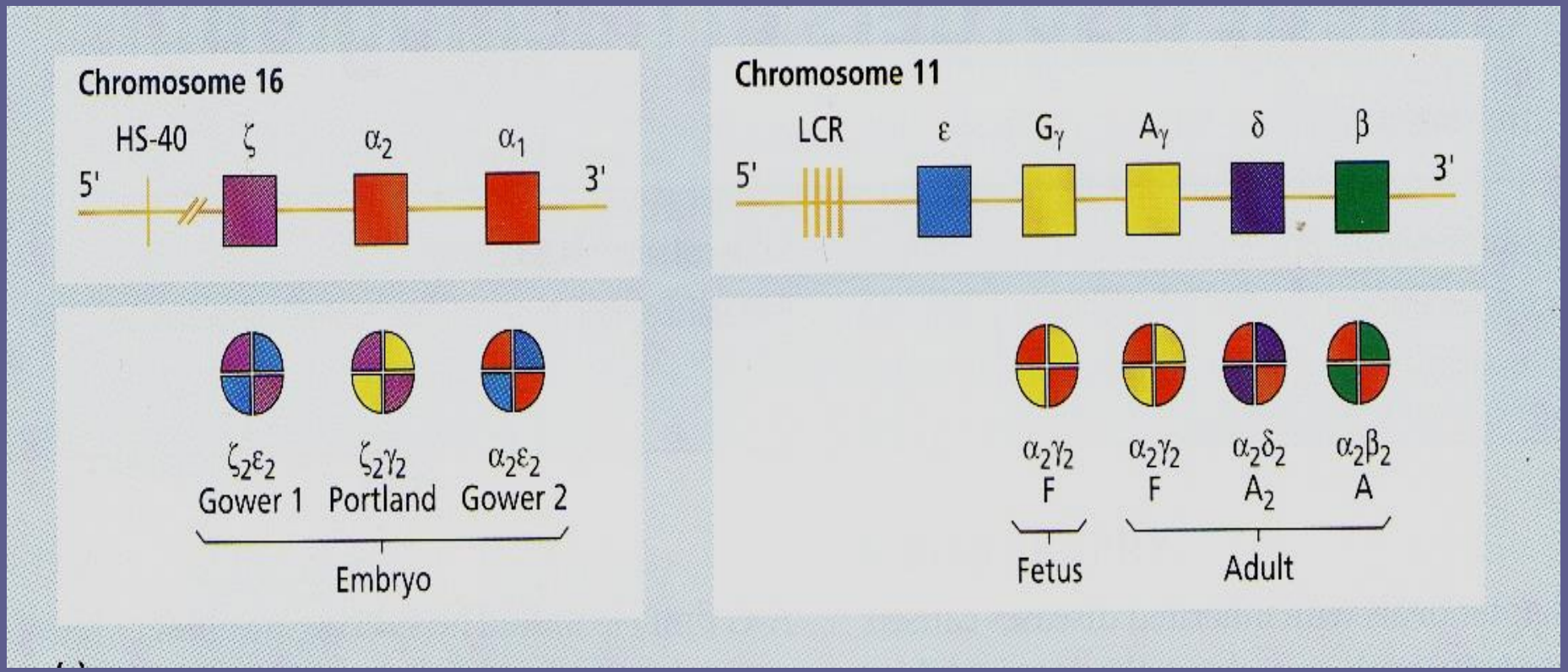


Synthesis of globin

- Various types of globin combines with haem to from different haemoglobin

- Eight functional globin chains, arranged in two clusters the
  - β- cluster (β, γ, δ and ε globin genes) on the short arm of chromosome 11
  - α- cluster (α and ζ globin genes) on the short arm of chromosome 16

Globin gene clusters

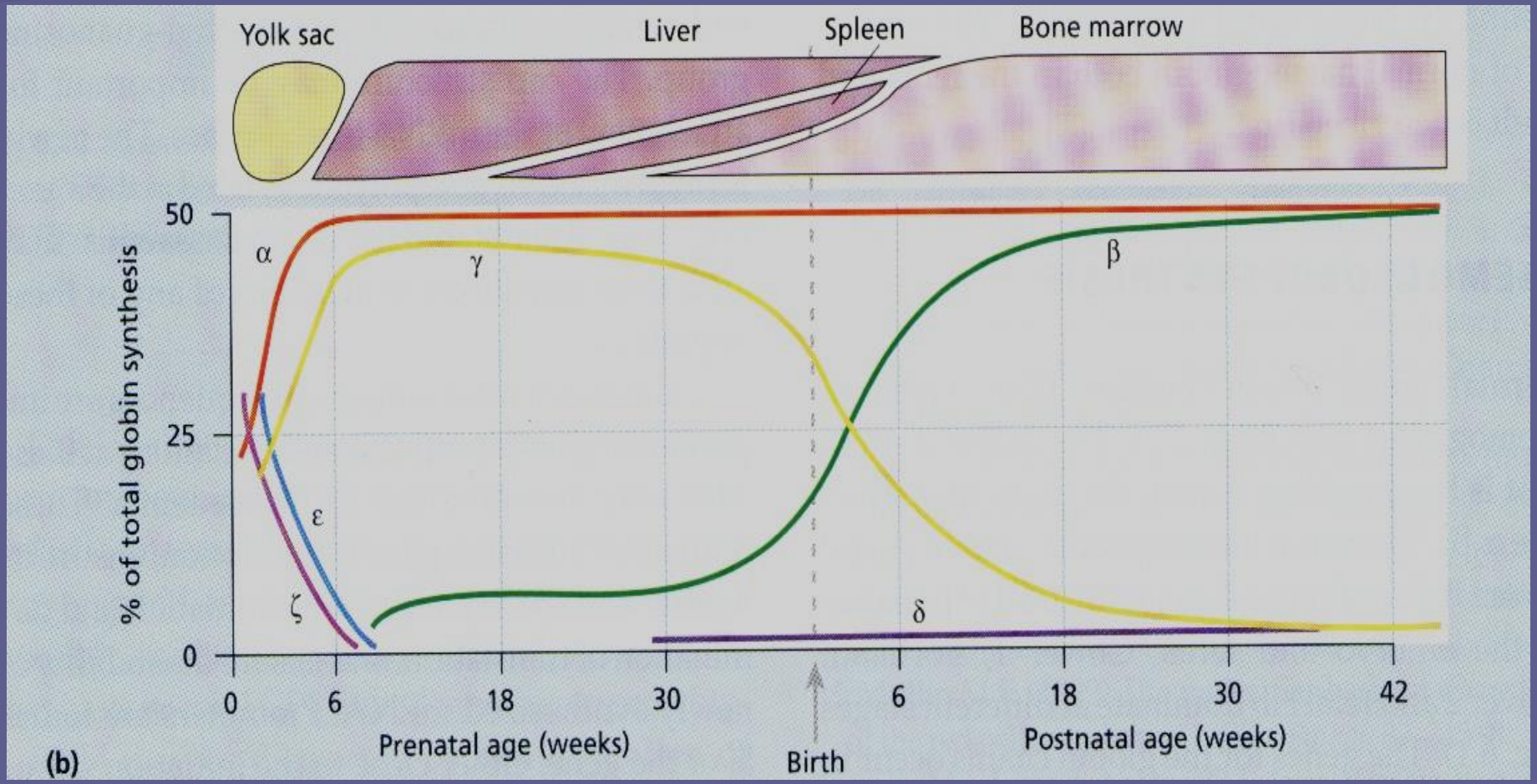


Synthesis of globin

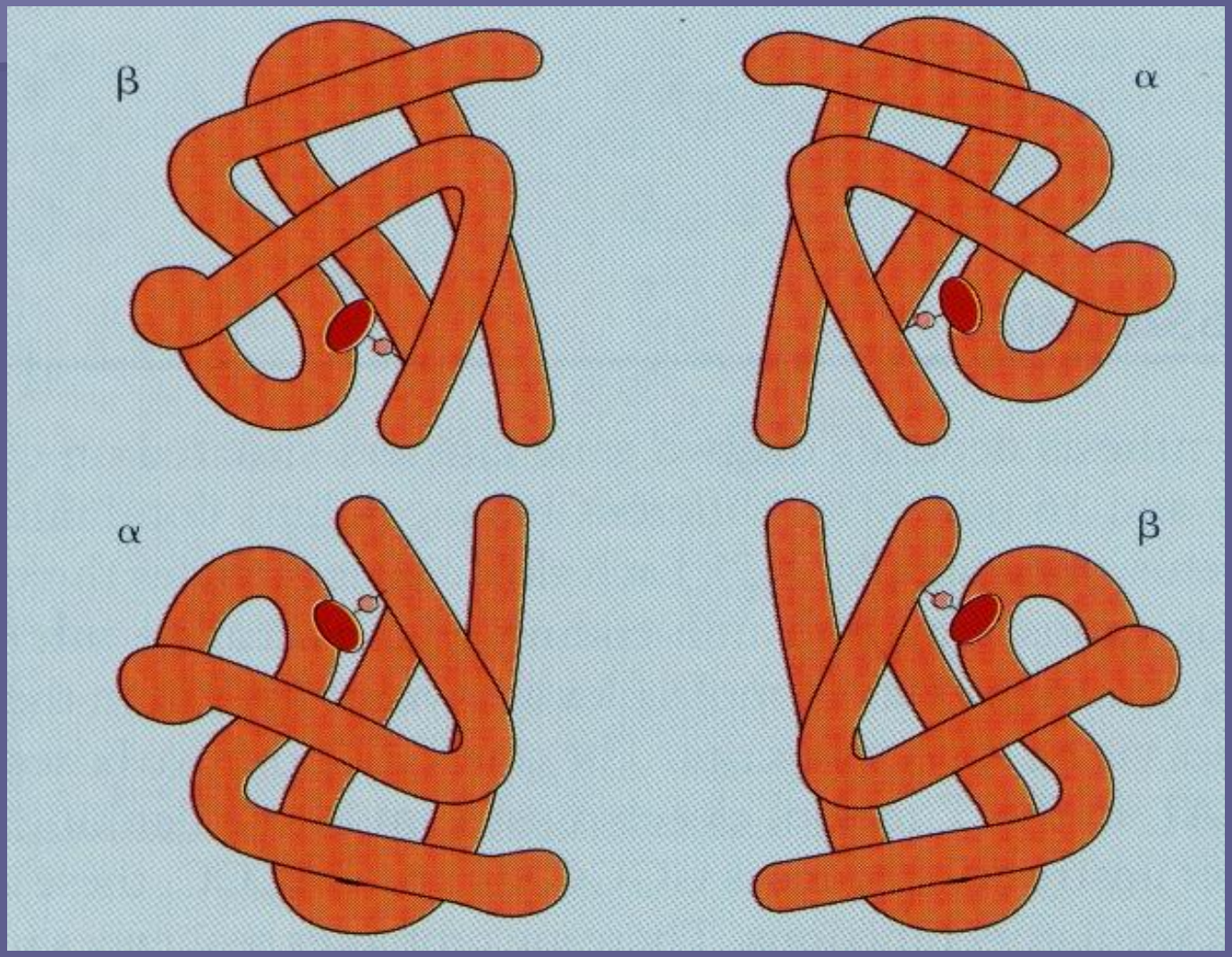
Globin synthesis, starts at 3rd week of gestation

- Embryonic
  - Haemoglobin Gower I ($\zeta_2\varepsilon_2$)
  - Haemoglobin Portland ($\zeta_2\gamma_2$)
  - Haemoglobin Gower II ($\alpha_2\varepsilon 2$)
- Fetal : HbF ($\alpha_2\gamma_2$), HbA ($\alpha_2\beta_2$)
- Adult : HbA, HbA2 ($\alpha_2\delta_2$), HbF.

Globin chain switch



Alpha & beta chains



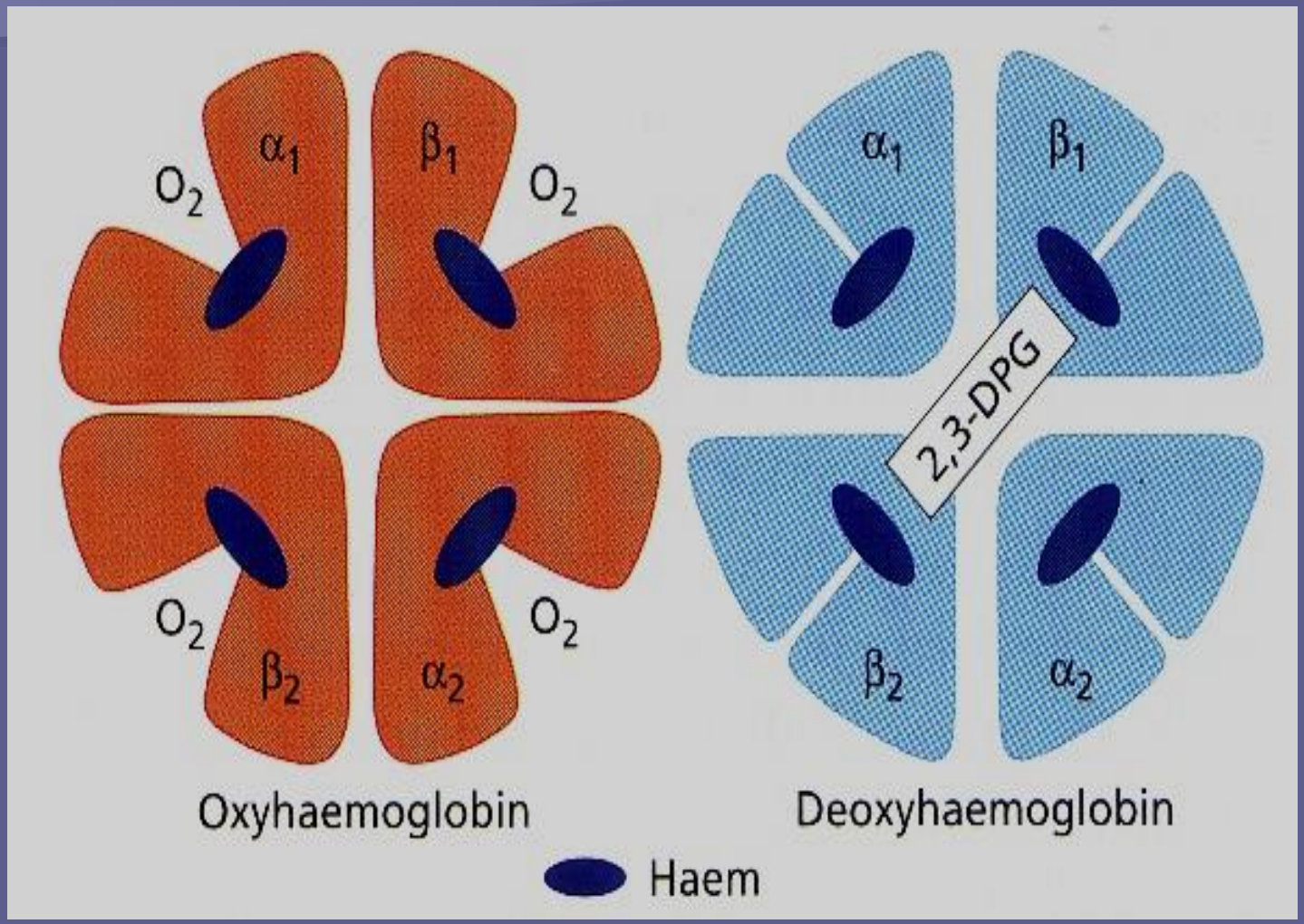
Adult haemoblobin

	Hb A	Hb A_2	Hb F
structure	$\alpha_2\beta_2$	$\alpha_2\delta_2$	$\alpha_2\gamma_2$
Normal %	96-98 %	1.5-3.2 %	0.5-0.8 %

Functions of Haemoglobin

- Oxygen delivery to the tissues
- Reaction of Hb & oxygen
  - Oxygenation not oxidation
  - One Hb can bind to four O_2 molecules
  - Less than .01 sec required for oxygenation
  - β chain move closer when oxygenated
  - When oxygenated 2,3-DPG is pushed out
  - β chains are pulled apart when O_2 is unloaded, permitting entry of 2,3-DPG resulting in lower affinity of O_2

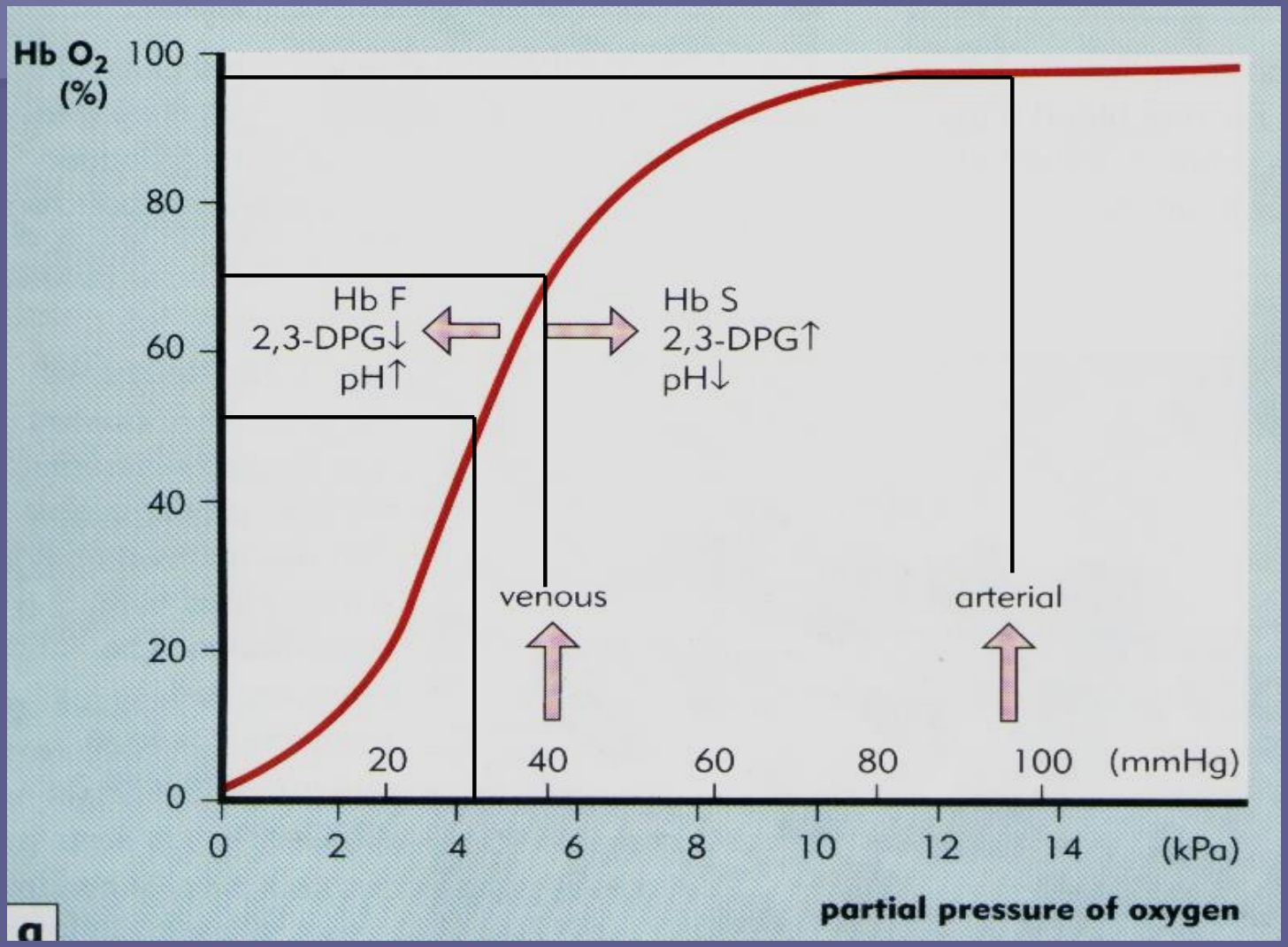
Oxy & deoxyhaemoglobin



Oxygen-haemoglobin dissociation curve

- O_2 carrying capacity of Hb at different Po_2
- Sigmoid shape
  - Binding of one molecule facilitate the second molecule binding
  - P_{50} (partial pressure of O_2 at which Hb is half saturated with O_2) 26.6mmHg

Hb-oxygen dissociation curve



Hb-oxygen dissociation curve

- The normal position of curve depends on
  - Concentration of 2,3-DPG
  - H^+ ion concentration (pH)
  - CO_2 in red blood cells
  - Structure of Hb

Hb-oxygen dissociation curve

- Right shift (easy oxygen delivery)
  - High 2,3-DPG
  - High H^+
  - High CO_2
  - HbS
- Left shift (give up oxygen less readily)
  - Low 2,3-DPG
  - HbF

Summary

- Normal structure including the proportion of globin chains are necessary for the normal function of haemoglobin
- Reduced haemoglobin in the red blood cells due to any abnormality of any of its constituents result into a clinical situation called anaemia
- Metabolic & other abnormalities result into abnormal oxygen supply to the tissue