HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : Physiology

LEC NO. : "2"

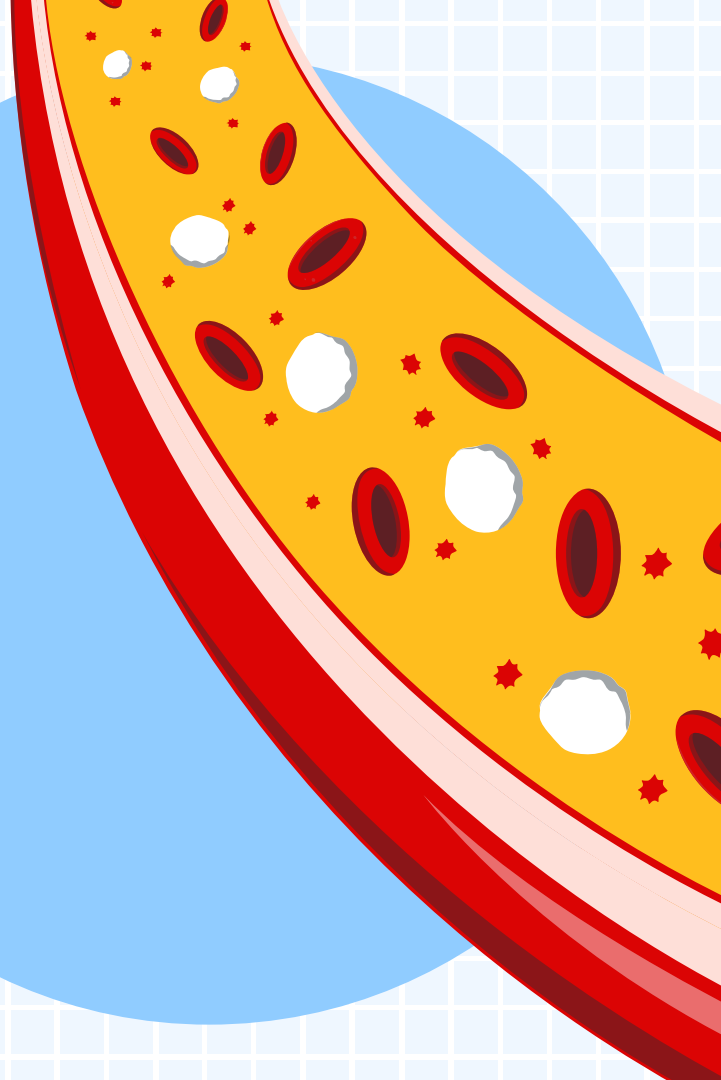
DONE BY : Zeyad tareq

وَقُل رَّبِّ زِدْنِي عِلْمًا

MODULE

HLS (HEMO & LYMPH)

Physiology Lectures
Lecture No. (2)
Slides By: Malek Hassan
Notes By:



مبدأيًا بدنا نعرف تركيبه ⇐ Hemoglobin من الإسم هو عبارة عن Heme + globin

Heme ⇒ Organic compound composed of porphyrin ring & in center ther is a Ferrous iron " Fe^{+2} " to which oxygen is attached.

should be ferrous to bind with oxygen.

Globin ⇒ Polypeptide chain composed from 4 chains

" رح تفصوها لقدام بالمحاضرة "

Types of Hemoglobin :-

1) Hb A ⇒ in adults.

2) Hb F ⇒ in ferus. Has higher affinity to O_2 than HbA. This good for fetus in uterus

3) Hbs ⇒ in anemia

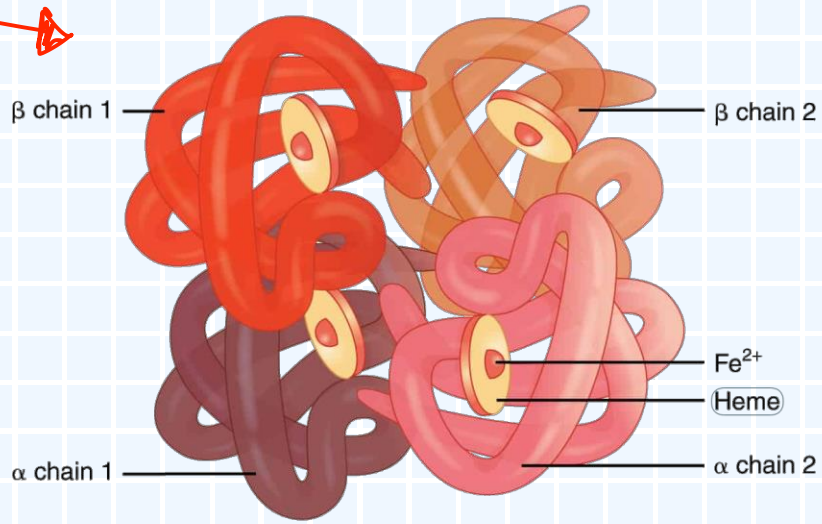
fetus has high 2,3 BPG & related to the curve slide 8

this will leads to ↓ the Hb-O_2 affinity & ↑ the releas of O_2 to tissues

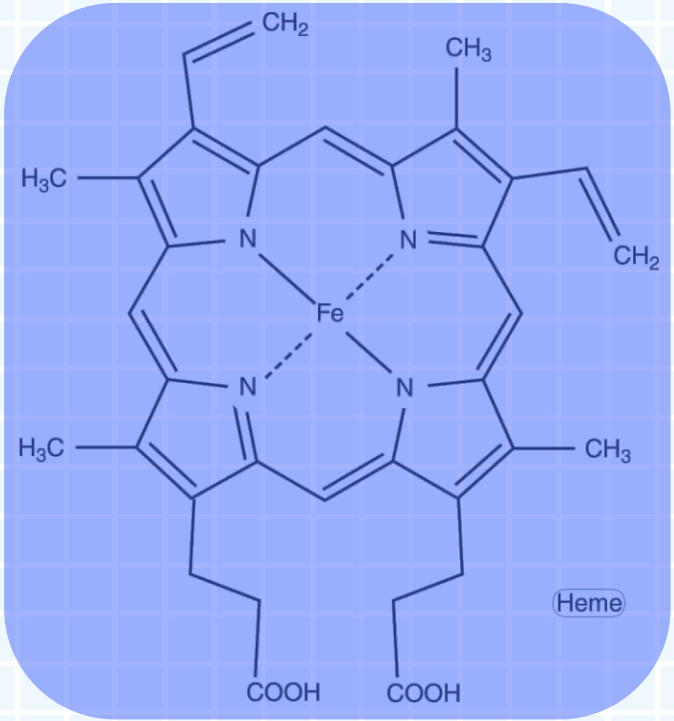
Hemoglobin:

Structure of Hemoglobin:

Adult Hemoglobin



(a)



(b)

Hemoglobin:

Reactions of Hemoglobin:

1. **Oxygenation**

The dynamics of the reaction of hemoglobin with O_2 make it a particularly suitable O_2 carrier. Hemoglobin is a protein comprised of four subunits, each containing a heme moiety attached to a polypeptide chain. In normal adults, most hemoglobin molecules contain two α and two β chains. Heme is a porphyrin ring complex that includes one atom of ferrous iron (Fe^{2+}). Each of the four iron atoms in hemoglobin can reversibly bind one O_2 molecule. The iron stays in the ferrous state, so the reaction is oxygenation (not oxidation). It has been customary to write the reaction of hemoglobin with O_2 as $Hb + O_2 \rightleftarrows HbO_2$. Because it contains four deoxyhemoglobin (Hb) units, the hemoglobin molecule can also be represented as Hb_4, and it actually reacts with four molecules of O_2 to form Hb_4O_8.

Every Hb has 4 heme groups & every heme group contains 1 Fe^{+2}

& therfore every Hb can carrying 4 Oxygen atoms.

The process of (oxygen, Fe^{+2}) binding is called Loading & depends on PO_2 (Partial pressure)

This reaction doesn't doesn't change the iron charge, but in oxidizing reactions it's changed to Fe^{+3} (ferric)

The affinity of Hb to O_2 is increasing gradually, so when 1st O_2 atom has lower affinity to Hb than 4th O_2 atom

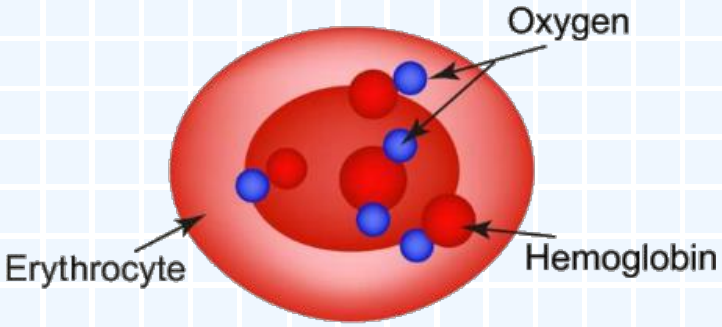
Tense & Relax state :- To understand them wath this video ⇒

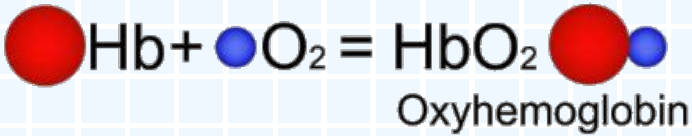
https://www.youtube.com/watch?v=XxElVpgNUF0&ab_channel=JamesMoss

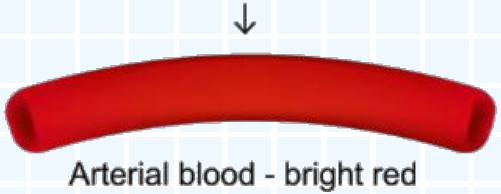
Hemoglobin:

Reactions of Hemoglobin:

1. **Oxygenation**







$$Hb_4 + O_2 \rightleftarrows Hb_4O_2$$

$$Hb_4O_2 + O_2 \rightleftarrows Hb_4O_4$$

$$Hb_4O_4 + O_2 \rightleftarrows Hb_4O_6$$

$$Hb_4O_6 + O_2 \rightleftarrows Hb_4O_8$$

Hemoglobin:

Reactions of Hemoglobin:

1. **Oxygenation**

The Oxygen–Hemoglobin dissociation curve relates the percentage saturation of the O_2-carrying power of hemoglobin (abbreviated as SaO_2) to the PO_2. Due to the T–R configuration interconversion, the curve has a characteristic sigmoid shape. Combination of the first heme in the Hb molecule with O_2 increases the affinity of the second heme for O_2, and oxygenation of the second increases the affinity of the third, and so on, so that the affinity of Hb for the fourth O_2 molecule is many times that for the first.

Hemoglobin:

Reactions of Hemoglobin:

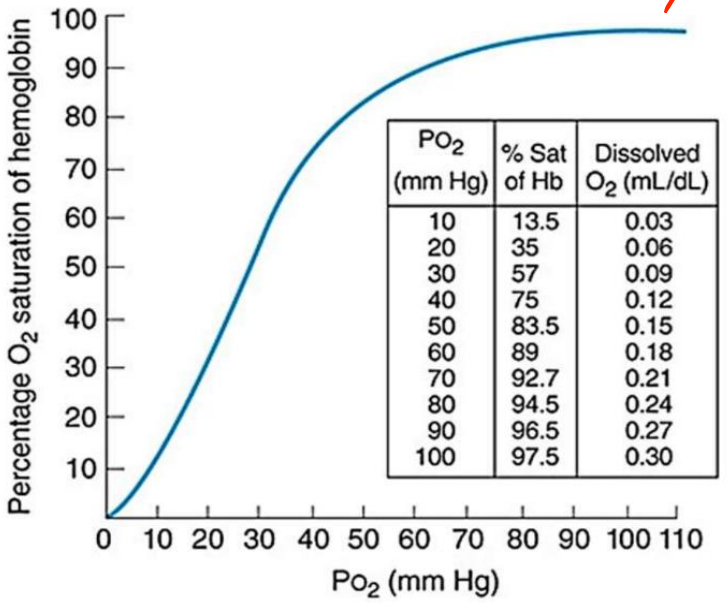
1. **Oxygenation**

The Oxygen–Hemoglobin dissociation curve

The curve is sigmoid in shape.

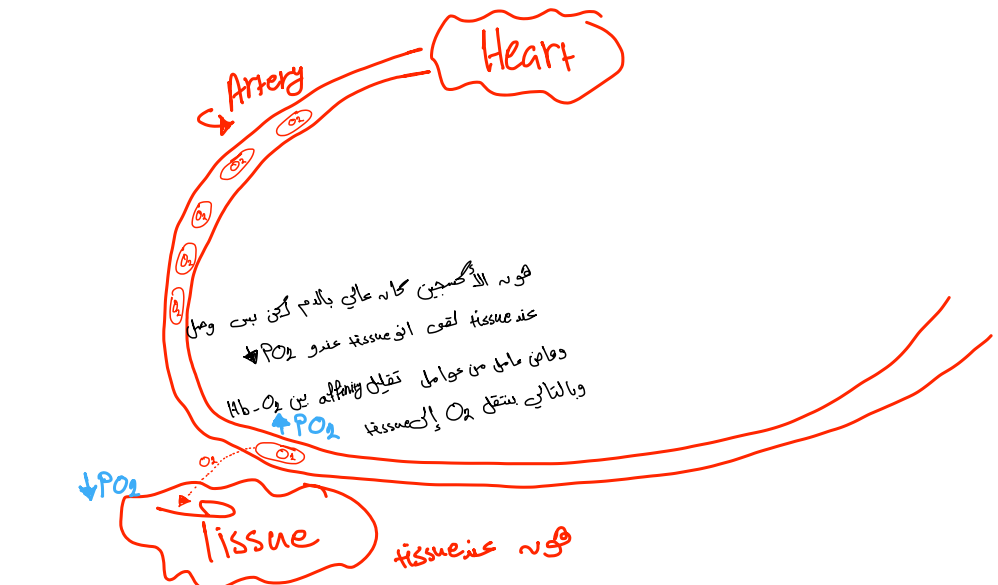
The curve isn't linear, why?!

because the affinity is variable.



PO_2 (mm Hg)	% Sat of Hb	Dissolved O_2 (mL/dL)
10	13.5	0.03
20	35	0.06
30	57	0.09
40	75	0.12
50	83.5	0.15
60	89	0.18
70	92.7	0.21
80	94.5	0.24
90	96.5	0.27
100	97.5	0.30

-1 **Oxygen–hemoglobin dissociation curve.** pH 7.40, temperature



هو عند tissue
ما فيه أكسجين والدم جاي بعطيه أكسجين
وبالتالي عند tissue بكون PO_2 قليل

Hemoglobin:

Reactions of Hemoglobin:

1. **Oxygenation**

   Factors that decrease the affinity between Oxygen & Hb shift the curve to the Right, while factors that increase the affinity between Oxygen & Hb cause a curve shift to the Left. The affinity of Hb for oxygen is decreased by (Release of oxygen = Shift to the Right):

   A. **Hydrogen ions, as they compete with oxygen for deoxygenated Hb.**

   B. **Rise of temperature.**

   C. **2, 3-diphosphoglycerate (2, 3-DPG) concentration (2,3-DPG is very plentiful in red cells. It is formed from 3- phosphoglyceraldehyde, a glycolysis product via the Embden–Meyerhof pathway. It is a highly charged anion that binds to the β chains of deoxyhemoglobin.**

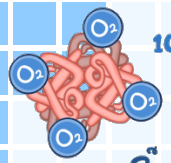
What will occur when Hb-O_2 complex faces CO?! The Hb can't releases O_2 & leads to hypoxia.

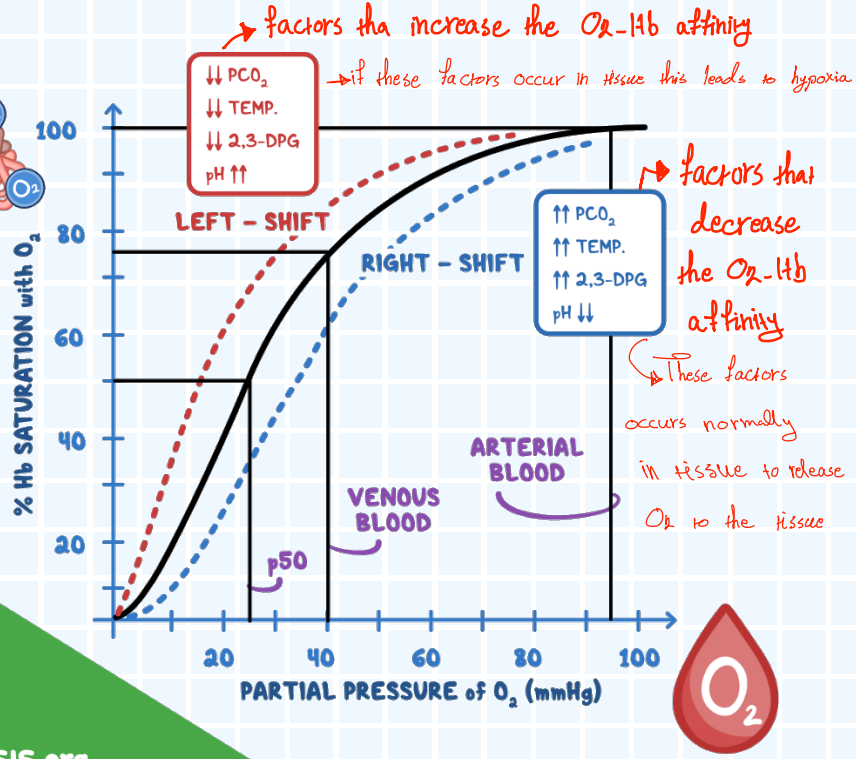
Hemoglobin:

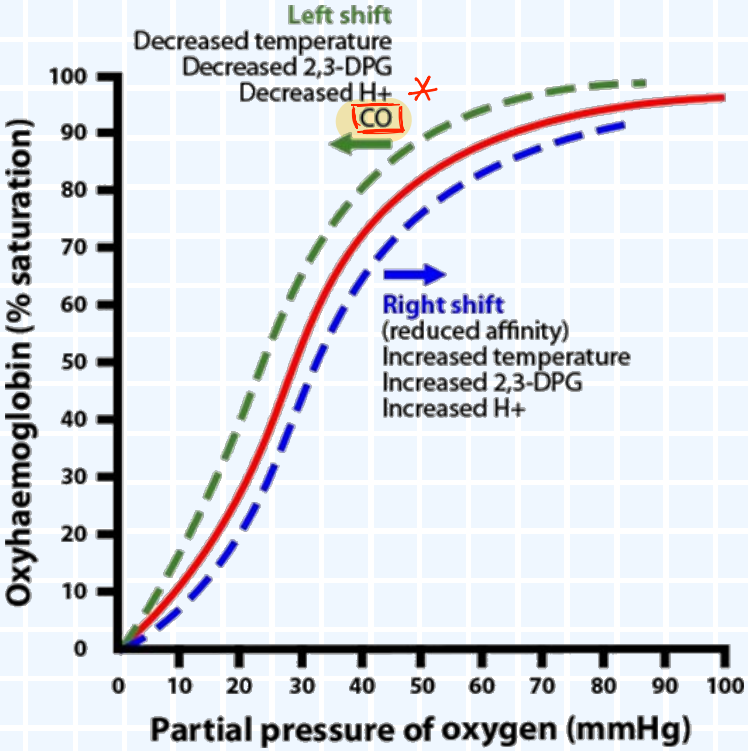
Reactions of Hemoglobin:

1. Oxygenation

CO → has more affinity to Hb than O_2





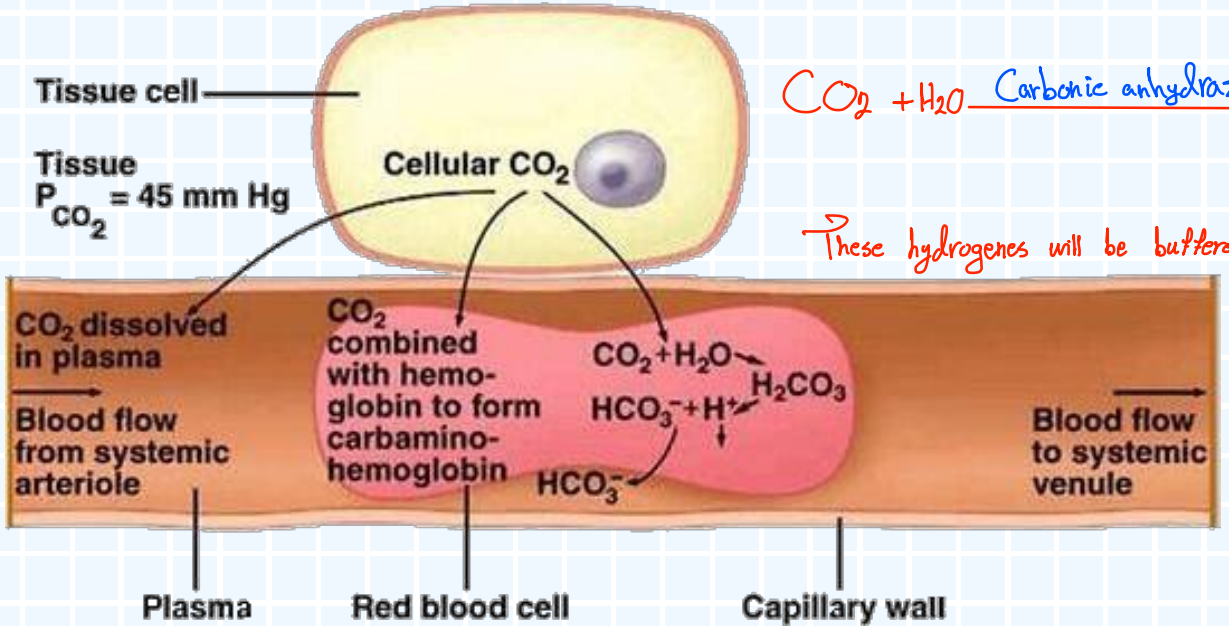


Hemoglobin:

Reactions of Hemoglobin:

2. With Carbon dioxide

- Hemoglobin combines with carbon dioxide to form Carbaminohemoglobin. This is one of the ways by which the carbon dioxide added to the blood at the tissues is transported to the lungs.



$CO_2 + H_2O$ — Carbonic anhydraze → $H_2CO_3 \rightarrow HCO_3^- + H^+$

These hydrogenes will be buffered by Hb to prevent changes in pH.

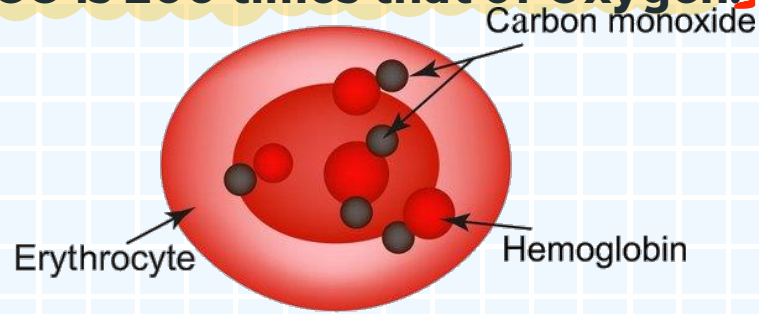
CO → called silent Killer.

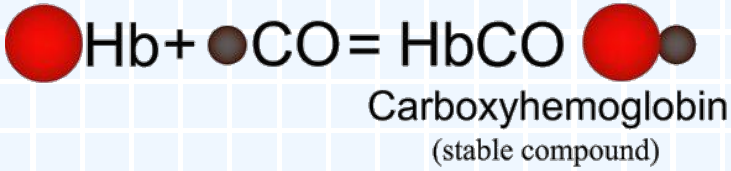
Hemoglobin:

Reactions of Hemoglobin:

3. With Carbon monoxide

Hemoglobin reacts with carbon monoxide (CO) to form Carboxyhemoglobin. CO combines with iron and displaces oxygen; thus, it prevents hemoglobin from carrying oxygen. The affinity of hemoglobin for CO is 200 times that of Oxygen.





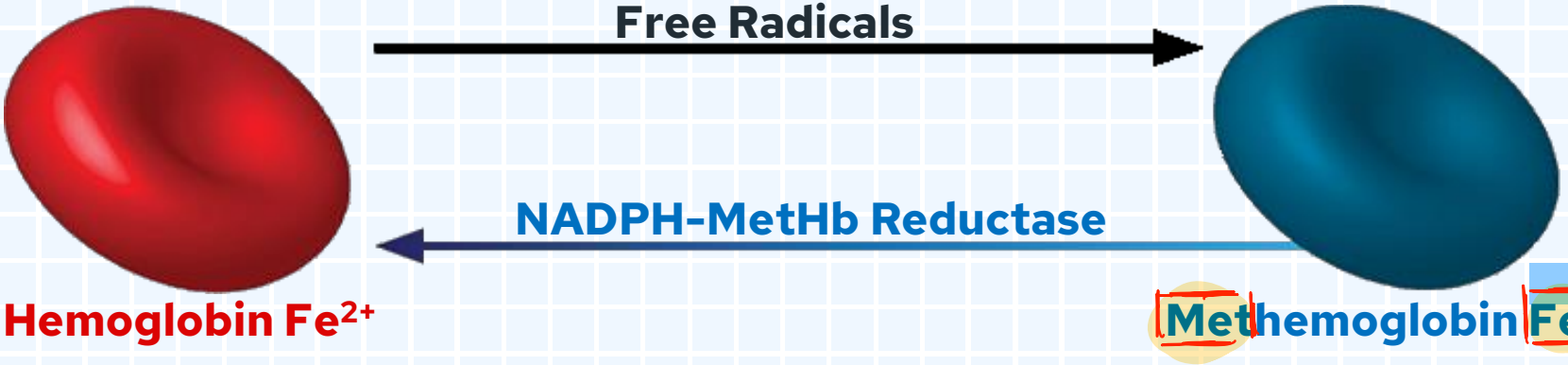
Carboxyhemoglobin cannot carry oxygen and carbon dioxide

Hemoglobin:

Reactions of Hemoglobin:

4. With Strong Oxidizing Agents

When hemoglobin is exposed to strong oxidizing agents, the Fe^{2+} iron is changed to Ferric Iron (Fe^{3+}), and the Hemoglobin is changed to dark-colored Methemoglobin, which cannot carry oxygen.
Small amounts of methemoglobin are normally formed but are reduced by NADH-MetHb Reductase back to hemoglobin.



هما طبيعيًا ارتباط $Hb + Fe^{+2}$ ما بغير خصت الـ Fe^{+2}

لكن مرات في عوامل موكسدة زي free radicals تحول Fe^{+2} to Fe^{+3}

والـ Fe^{+3} ما بقدر يحمل اكسجين لحل واي المشكلة فيه NADPH بحول Fe^{+3} to Fe^{+2}

HbA1C → السكر التراكمي

it's called "Glycated hemoglobin" it's range lower 4.5 % of HbA

if it increases this indicated chronic hyperglycemia

Hemoglobin:

Types of Hemoglobin :

1. **Adult hemoglobin (HbA):**

   In Normal Adult Human hemoglobin (hemoglobin A), the two polypeptides are α chains and β chains. Thus, hemoglobin A is designated α2β2. Not all the hemoglobin in the blood of normal adults is hemoglobin A. less than 3% of the total Hb is HbA2, in which β chains are replaced by δ chains (α2δ2).

   Small amounts of hemoglobin A derivatives closely associated with hemoglobin A represent glycated hemoglobin. One of these, hemoglobin A1c (HbA1c), has glucose attached to the terminal valine in each β chain and is of particular interest because it increases in the blood of patients with poorly controlled diabetes mellitus and is measured clinically as a marker of the progression of that disease and the effectiveness of treatment.

2. **Fetal hemoglobin (HbF):**
3. **Other:**

Hemoglobin:

Types of Hemoglobin :

1. **Adult hemoglobin (HbA):**
2. **Fetal hemoglobin (HbF):**

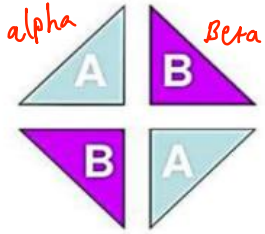
   The blood of the Human Fetus normally contains fetal hemoglobin (Hemoglobin F). Its structure is like that of hemoglobin A except that γ chains replace the β chains; that is, hemoglobin F is α2γ2. The cause of this greater affinity is the poor binding of 2,3-DPG by the γpolypeptide chains that replace β-chains in fetal hemoglobin. Fetal hemoglobin is normally replaced by adult hemoglobin soon after birth. Hemoglobin F is, therefore, critical to facilitate the movement of O_2 from the maternal to the fetal circulation.

3. **Other:**

   In Young Embryos, there are Gower 1 hemoglobin and Gower 2 hemoglobin. Switching from one form of hemoglobin to another during the development

Hemoglobin:

Types of Hemoglobin : → This because difference in polypeptide chain

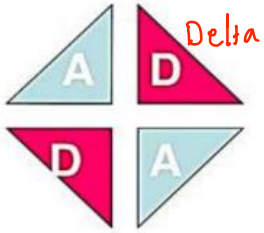


in adults

HbA

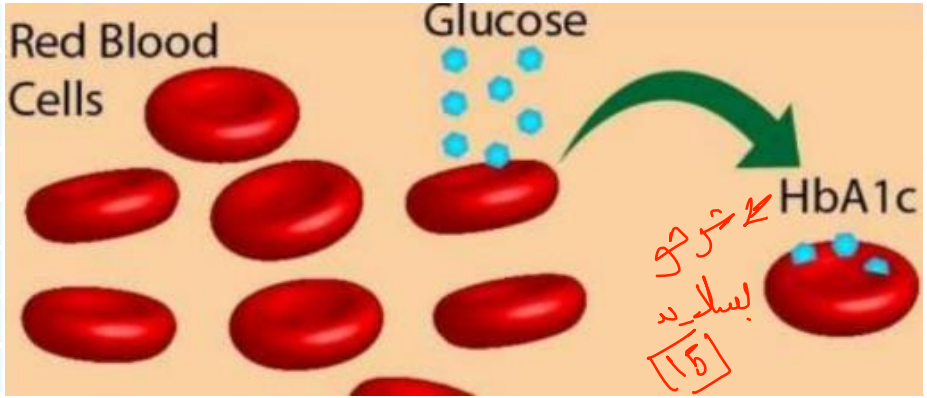
in fetus

HbF

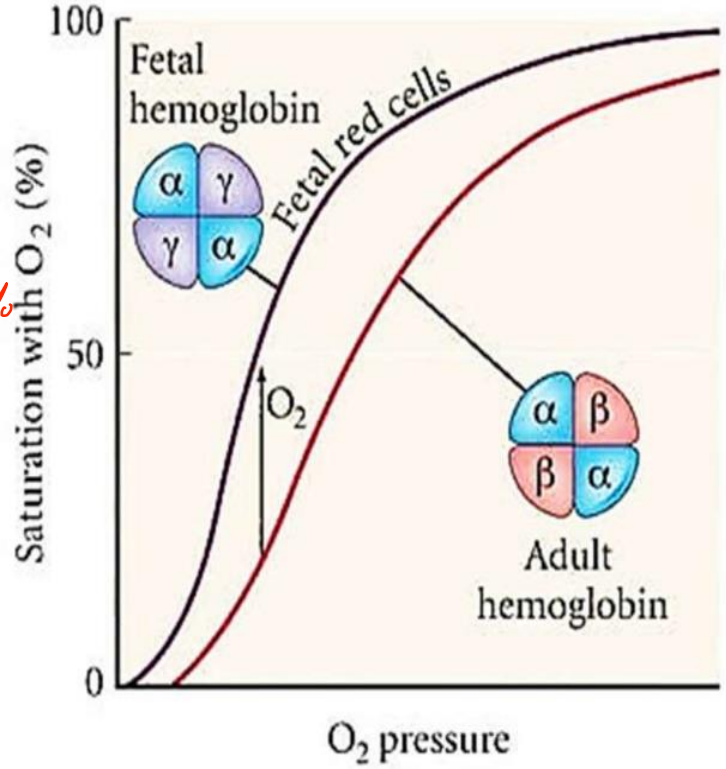


in adults 2%

HbA_2

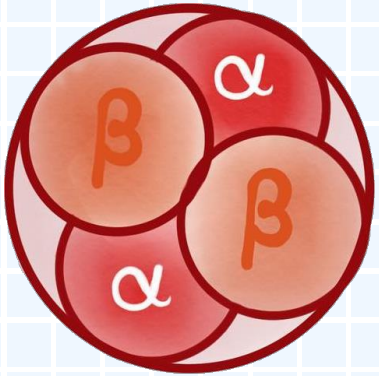


خرجي بسلايد [15]



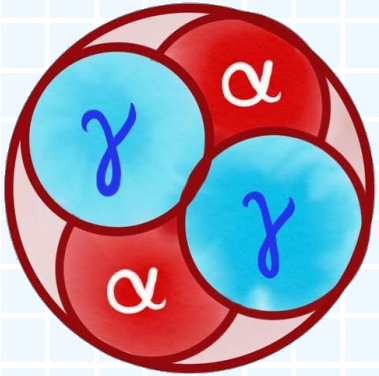
Hemoglobin:

Types of Hemoglobin :



Adult Haemoglobin
Hb A

2 x Beta chains
2 x Alpha chains



Fetal Haemoglobin
Hb F

2 x Gamma chains
2 x Alpha chains

Functions of RBCs

Functions of Hemoglobin :

1. **The transport of Oxygen from lungs to tissues & Carbon dioxide** (involving CA enzyme reaction) from tissues to lungs is the most important function of RBCs. Carbonic Anhydrase in RBCs converts the carbon dioxide taken up by them:

2. **Hemoglobin is an important buffer.**
   It has Six Times more buffering power than plasma proteins. Therefore, it can buffer H^+ inside RBCs (formed during CO_2 transport) and can carry CO_2 with minimal change in pH. Hemoglobin-Carrying CO_2 (deoxyHb) is a stronger buffer than Hemoglobin-Carrying O_2 since deoxyHb dissociates less (i.e., it forms a Weaker Acid = a Stronger Buffer).

Functions of RBCs membrane

Keeps Hb inside RBCs

What is the hazard of free Hb?! fetal, why ?!

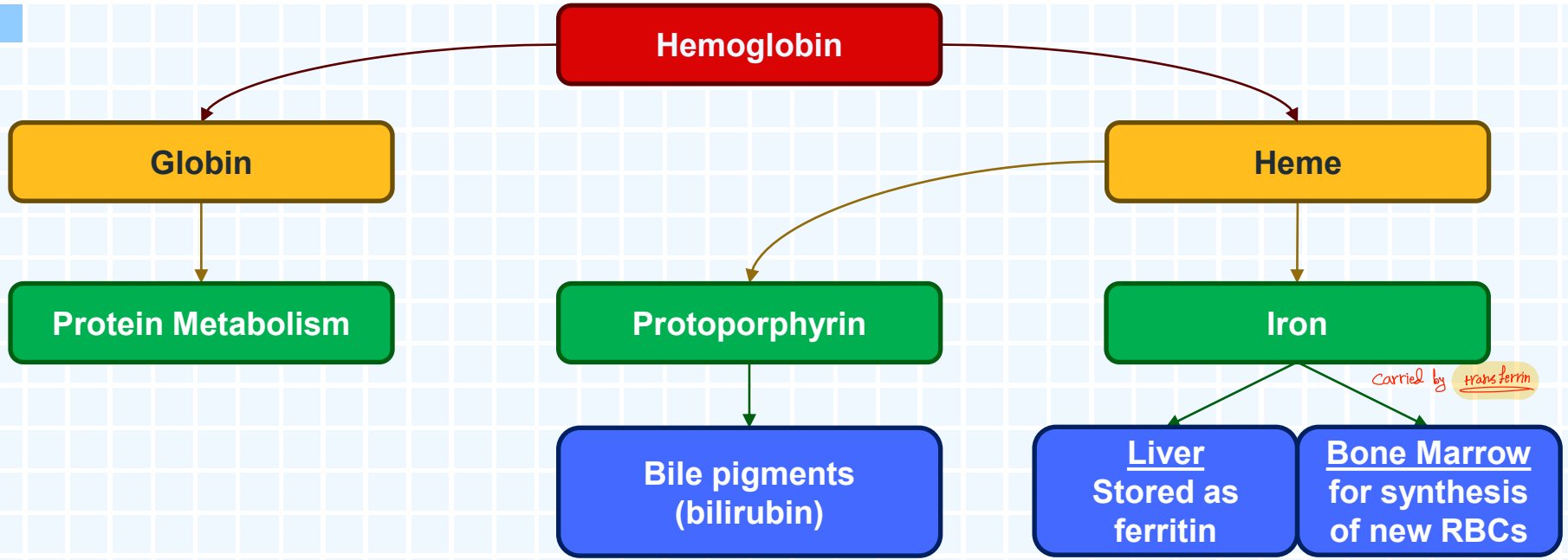
1) leads to Renal failure because Hb accumulates inside renal tubules

2) ↑ blood viscosity & therfore ↑ blood pressure & increase the workout on hurt muscle ⇒ leads to heart failure

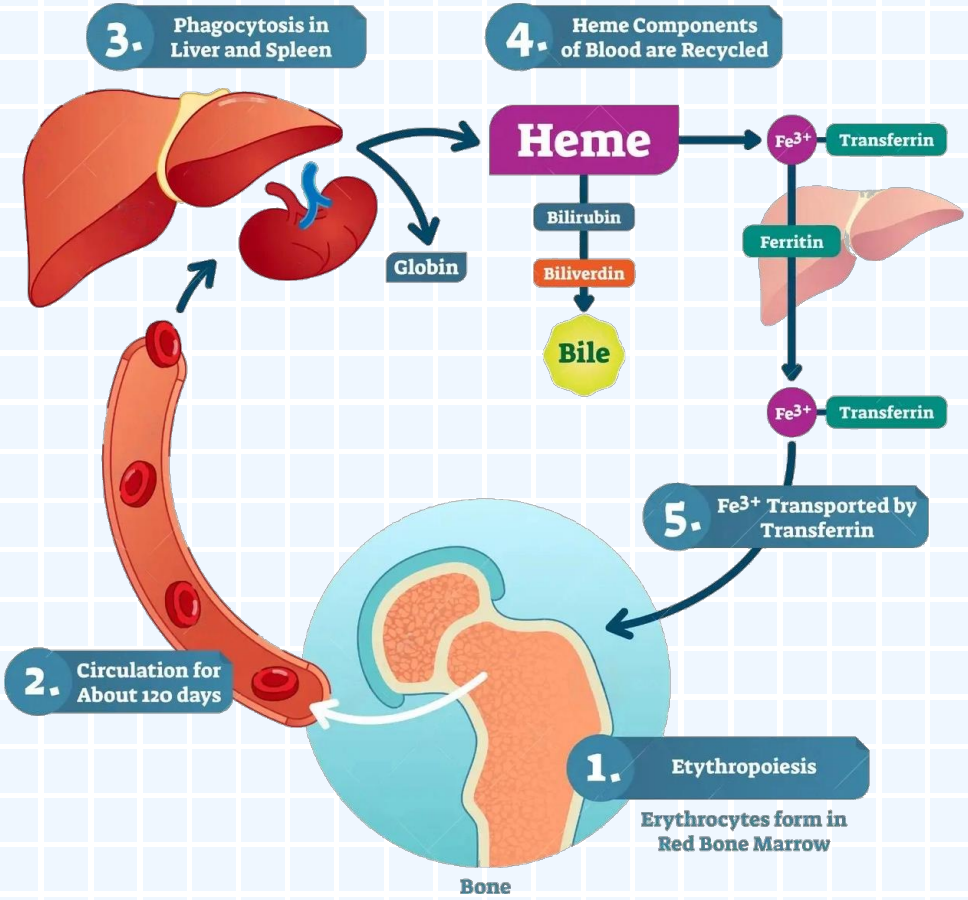
Life Span and Fate of RBCs

The life span of RBCs is 120 days. Old RBCs have fragile walls, which rupture easily when RBCs pass through very narrow blood vessels, especially in the spleen.

Hemoglobin is rapidly captured by the cells of the RES and broken into:



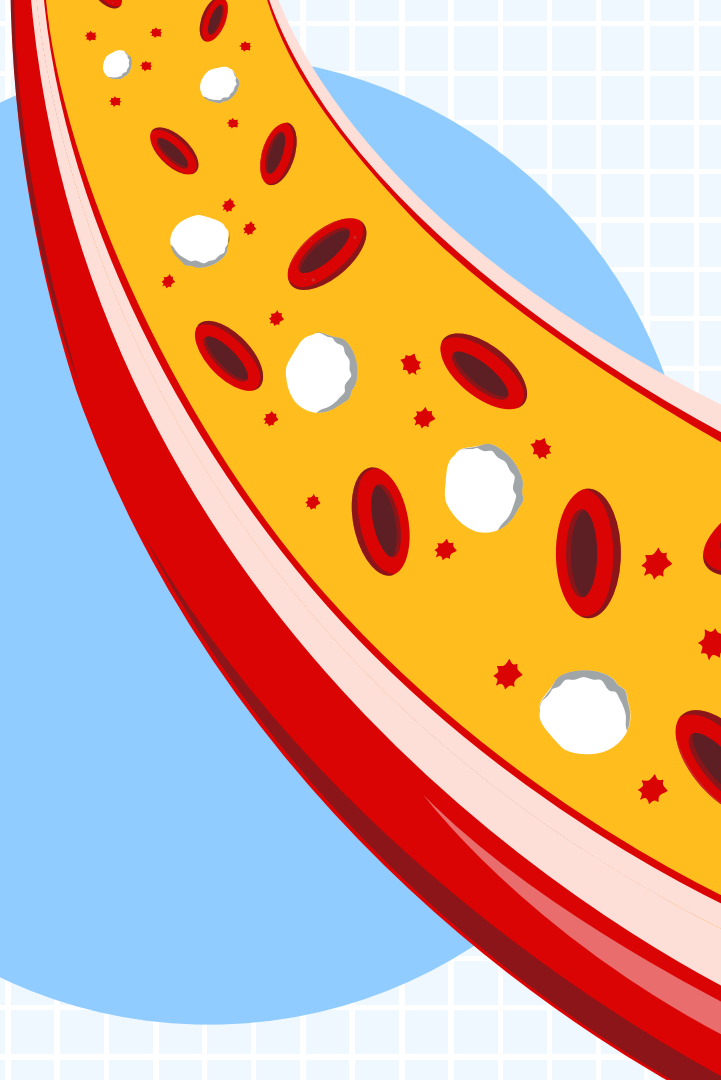
Life Span and Fate of RBCs




THANK
YOU
النادي الطبي

MODULE
HLS (HEMO & LYMPH)

Physiology Lectures
Lecture No. (3)
Slides By: Malek Hassan
Notes By:



ERYTHROPOIESIS

Definition: It is the process of formation of new RBCs.

Sites of Erythropoiesis:

- **In the Fetus:** RBCs are formed in the liver and spleen. & yolc sac
- **After Birth:** RBCs are formed in the red bone marrow of long bones.
- **By the age of 20:** The red bone marrow in long bones becomes replaced by fatty tissue and cannot produce RBCs.
- **After the age of 20:** The bone marrow of flat membranous bones, such as ribs, vertebrae, pelvis, sternum, and skull, produce RBCs.

ERYTHROPOIESIS

Middle Trimester of Gestation

Liver
Spleen
Lymph Nodes

Last Trimester After Birth

Red bone marrow
(Bone marrow of all bones)

After 20

Membranous bones:
Vertebrae
Sternum
Ribs
Ilia