

# 8

## Blood physiology

- Very important
- Extra information
- Terms

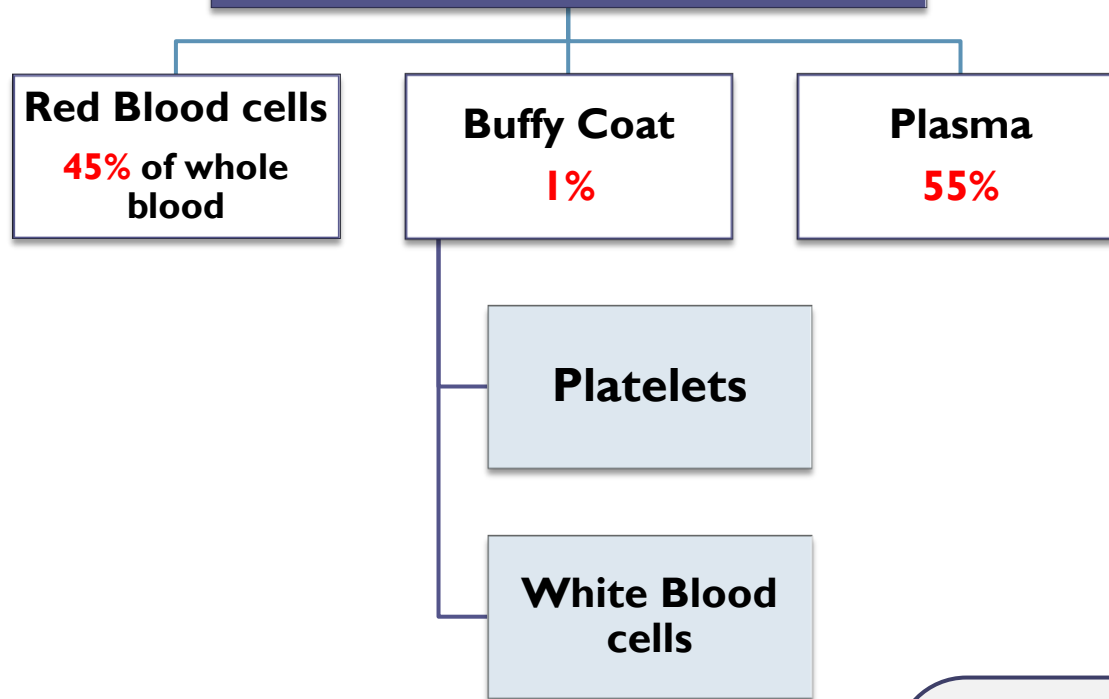
ملاحظة : تم دمج محاضرتي كريات الدم الحمراء لارتباطها الوثيق ببعضها الآخر

( نَلِكْ عَالَمُ الْغَيْبِ وَالشَّهَادَةِ الْعَزِيزُ الرَّحِيمُ \* الَّذِي أَحْسَنَ كُلَّ شَيْءٍ خَلَقَهُ وَبَدَأَ خَلْقَ الْإِنْسَانِ مِنْ طِينٍ \* ثُمَّ جَعَلَ نَسْلَهُ مِنْ سَلَالَةٍ مِنْ مَاءٍ مَهِينٍ \* ثُمَّ سَوَّاهُ وَنَفَخَ فِيهِ مِنْ رُوحِهِ وَجَعَلَ لَكُمُ السَّمْعَ وَالْأَبْصَارَ وَالْأَفْئِدَةَ قَلِيلًا مَّا تَشْكُرُونَ ) [السجدة: ٦ - ٩].

# Objectives:

- **At the end of this lecture you should be able to:**
- **Describe Cellular and non-cellular components of blood.**
- **Recognize functions of blood.**
- **Define Erythropoiesis; leucopoiesis, thrombopoiesis.**
- **Recognize sites of RBC formation at different developmental age.**
- **Describe different stages of RBC differentiation.**
- **Describe features of RBC maturation.**
- **Describe regulation of RBC production and erythropoietin hormone secretion in response to hypoxia.**
- **Recognize clinical conditions associated with high level of erythropoietin in the blood.**

# Blood composition



**The hematocrit** is the proportion, by volume, of the blood that consists of [red blood cells](#).

The hematocrit (HCT) is expressed as a percentage of the volume of whole blood that is made up of red blood cells. This measurement depends on [the number of red blood cells](#).

Hematocrit is also called packed-cell volume (PCV).

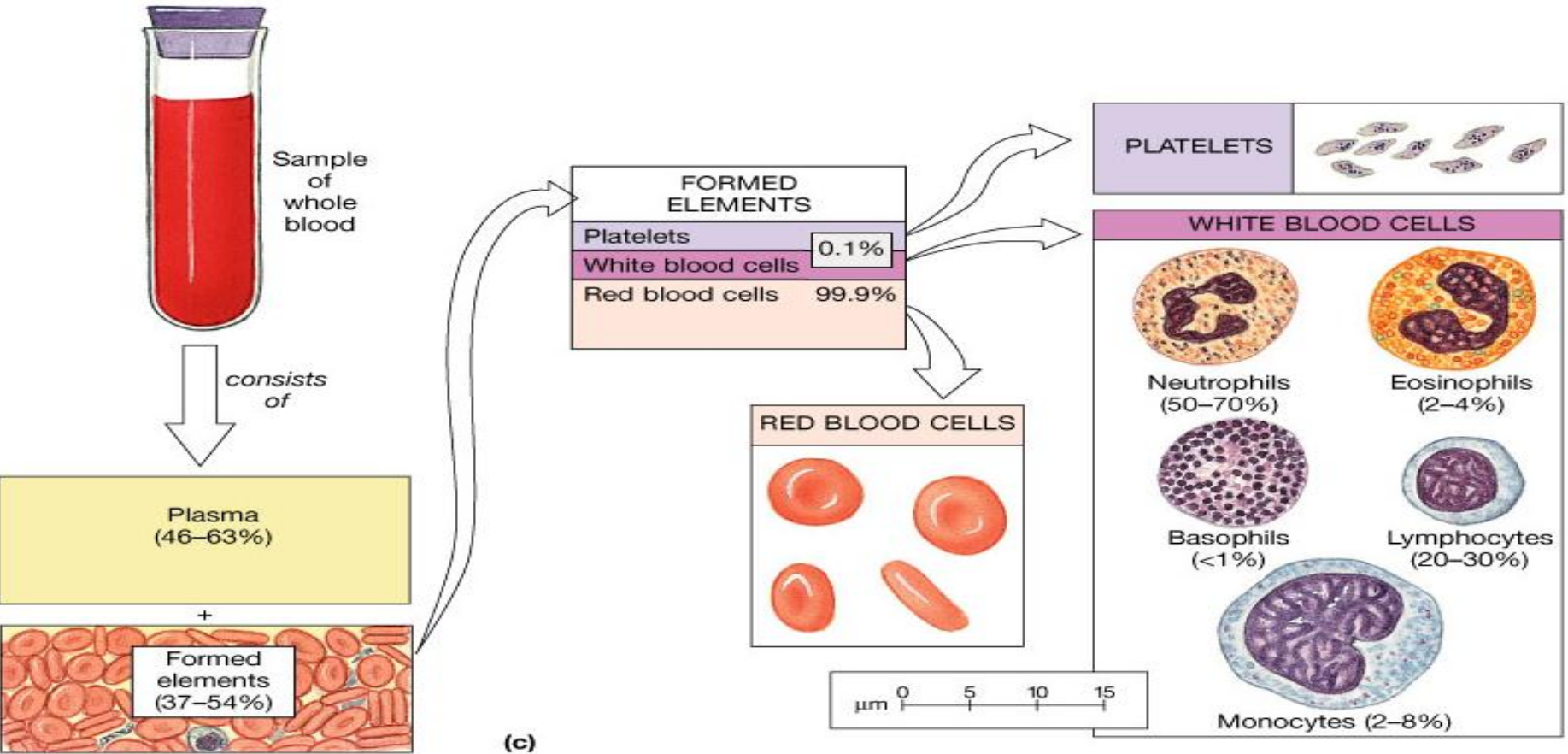
For better understanding see :

[Video1](#) & [Video2](#) & [Video3](#)

**Note:** the hematocrit differs from males to females. Males have more blood cells because females lose every month half a liter from blood.

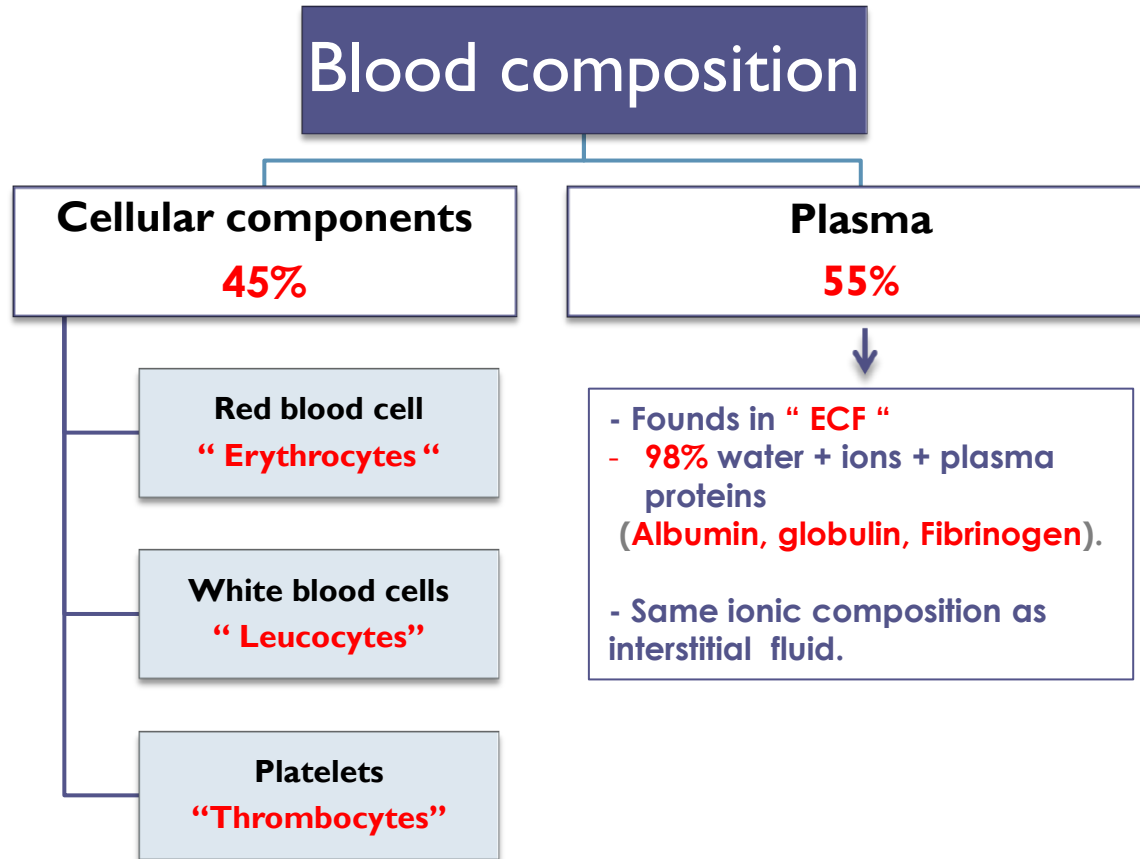
\* Hematocrit is from  
38% to 46% in females,  
42% to 54% in males.

\* Buffy coat is a hazy layer



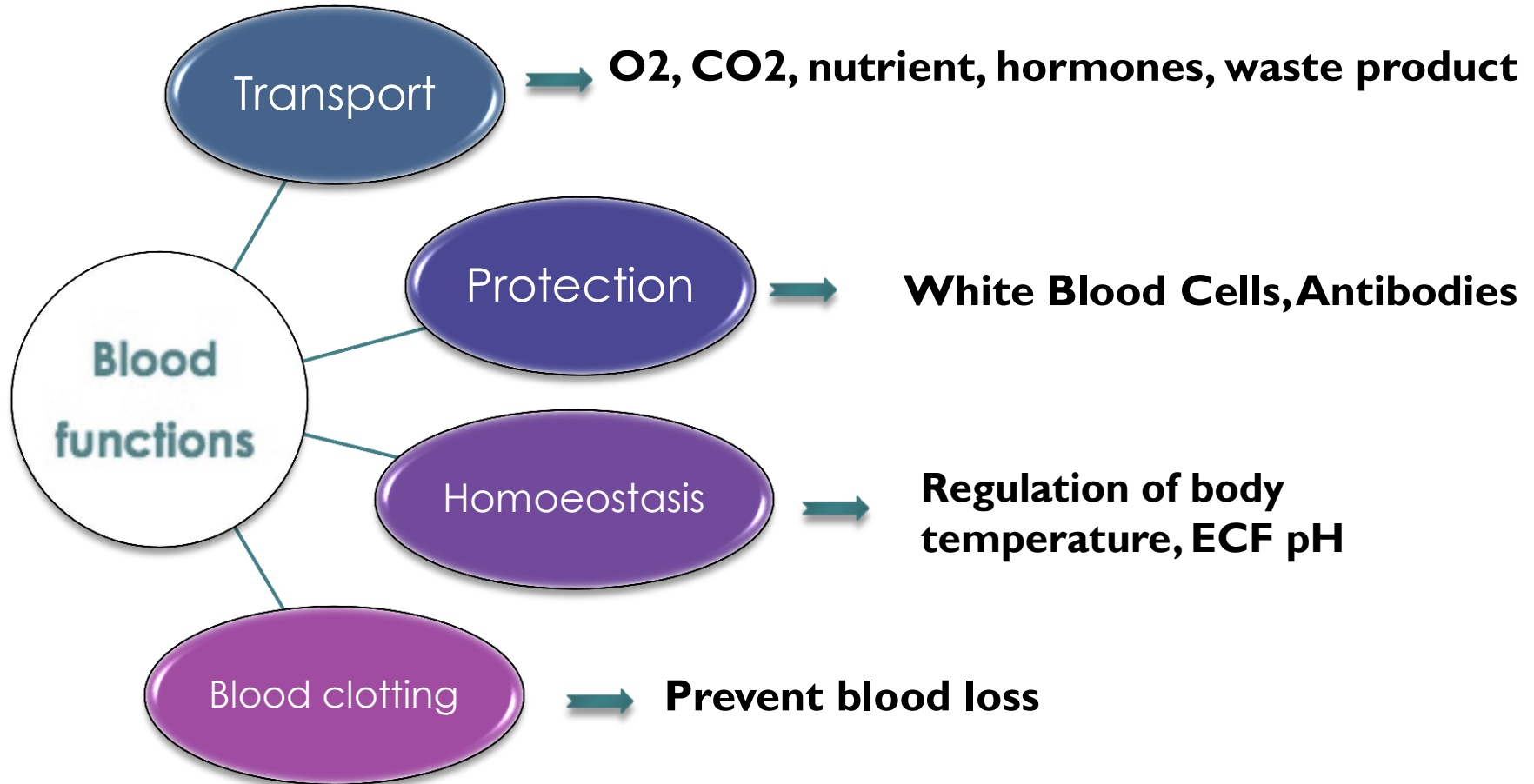
- **Note:** : red blood cells are in millions while white blood cells are in thousands
- red blood cells and platelets do not have nucleus. White blood cells have nucleus.
- The reason that the RBC don't have nucleus is to do its function efficiently

# Blood composition



**Note:** erytho = red , leuco = white  
- plasma has more protein than the interstitial fluid

# Function of blood

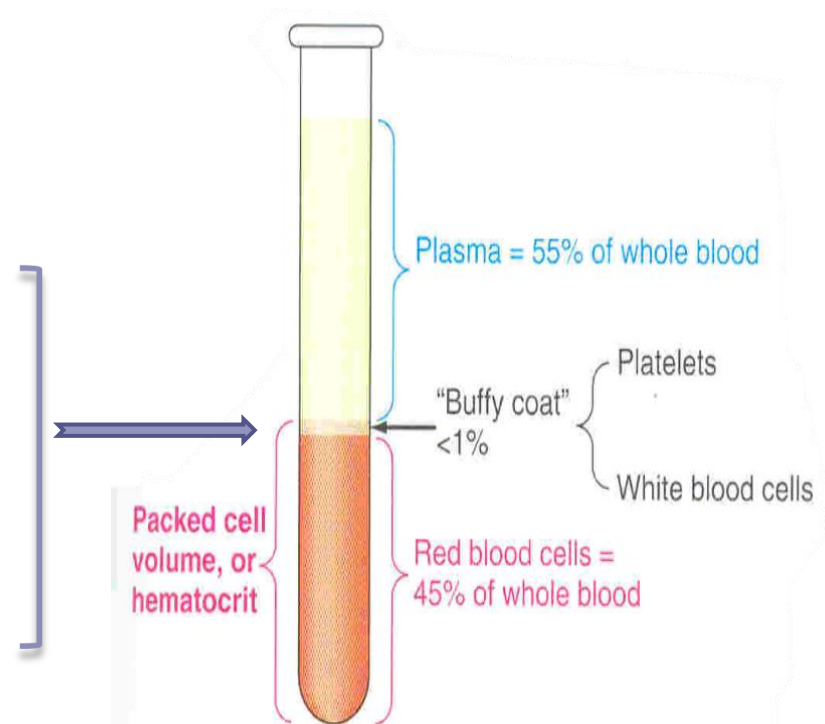


- ▶ **5 liter** in adult
  - 45% is packed cells volume (PCV).
  - 55% is plasma volume.

**Blood percentage higher in male more than female**

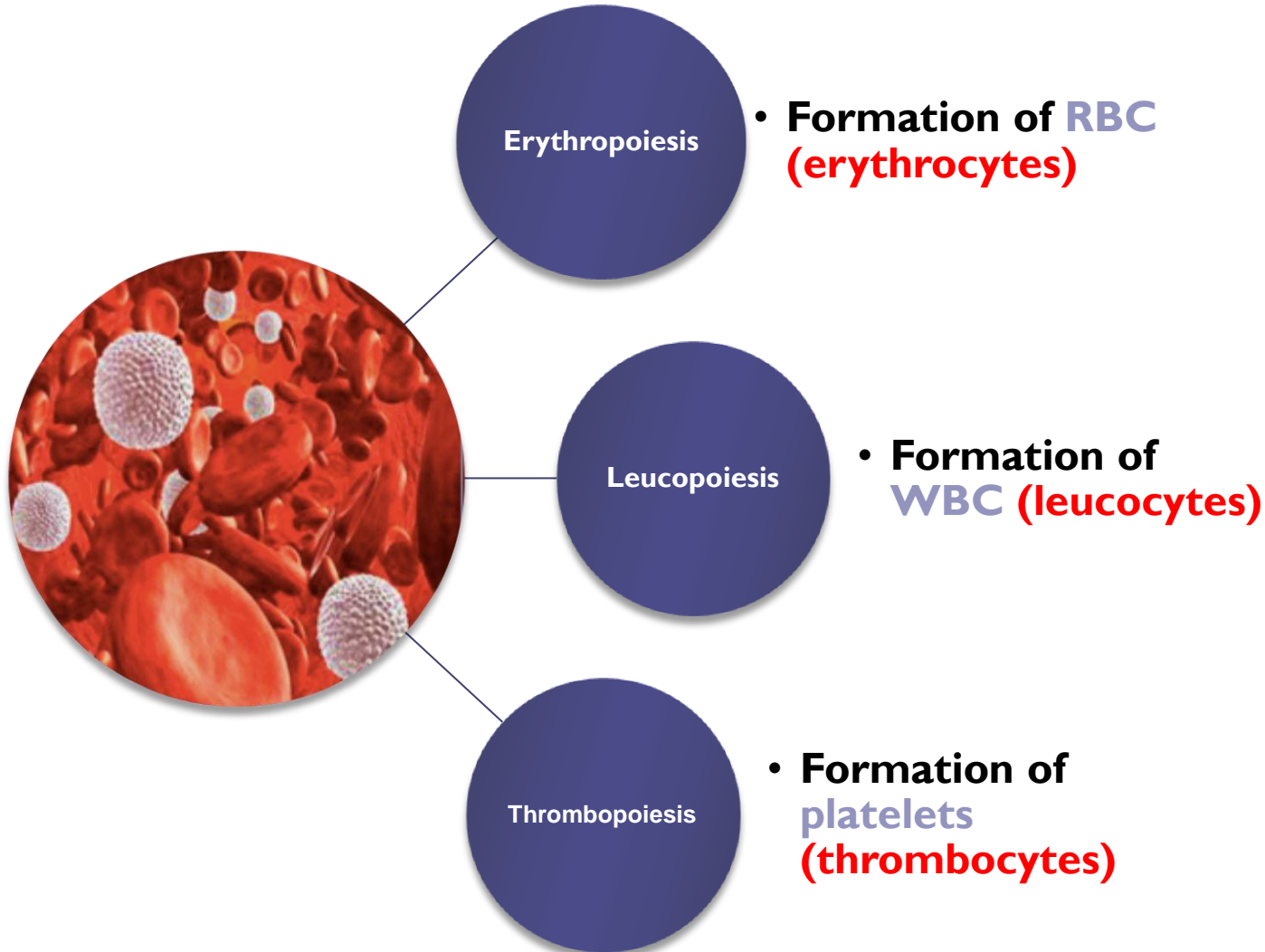
“ to compare between two person they should have the same size + age “

**When you leave a blood sample for a period of time, the RBC will be separated from the plasma ‘so the RBC becomes in the bottom of the tube “ in red color“ and the plasma at the top of the tube ” in yellow color“**





# Blood cells formation





## Red blood cells (RBC)

### Function

Buffer

CO<sub>2</sub> transport

O<sub>2</sub> transport

### Shape and size

- Flat Biconcave Disc.
- Non-nucleated.
- Diameter 7-8  $\mu\text{m}$  x 2.5  $\mu\text{m}$  x 1  $\mu\text{m}$ .
- Flexible.
- Average volume 90-95  $\mu\text{m}^3$
- Number = 4.7 - 5 x 10<sup>6</sup>
- Hb = 14-16 g/dl in the blood  
( Hb = Hemoglobin )

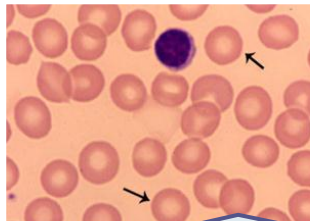


# RBCs Size, Color, Indices

## According to size :



**Microcytes**  
( small sized RBCs)

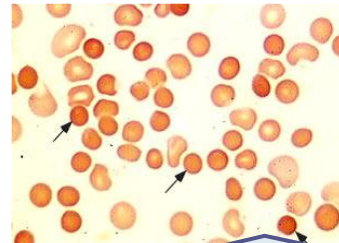


**Normocytes**  
( Normal sized RBCs)

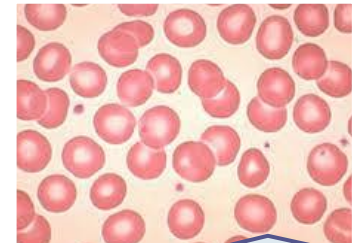


**Macrocytes**  
( Large sized RBCs)

## According to color :



**Hyperchromia**  
( Darker due to **increased** Hb)



**Normochromia**  
(Normal colored RBCs)



**Hypochromia**  
(paler due to **decreased** Hb)

شاحب = paler / Hb = hemoglobin / الصور خارجية وللإيضاح فقط

They are determined by measuring the indices:

## Mean corpuscular Volume :

“The average red blood cell size”

(**MCV= 78 to 94 fl or 83 Cubic um**)

## Mean corpuscular hemoglobin :



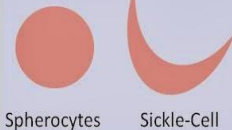
“The amount of hemoglobin per red blood cell”

(**MCH= 27 – 32 picogram**)

## Mean corpuscular hemoglobin concentration :

“The amount of hemoglobin relative to the size of the cell or hemoglobin concentration per red blood cell”

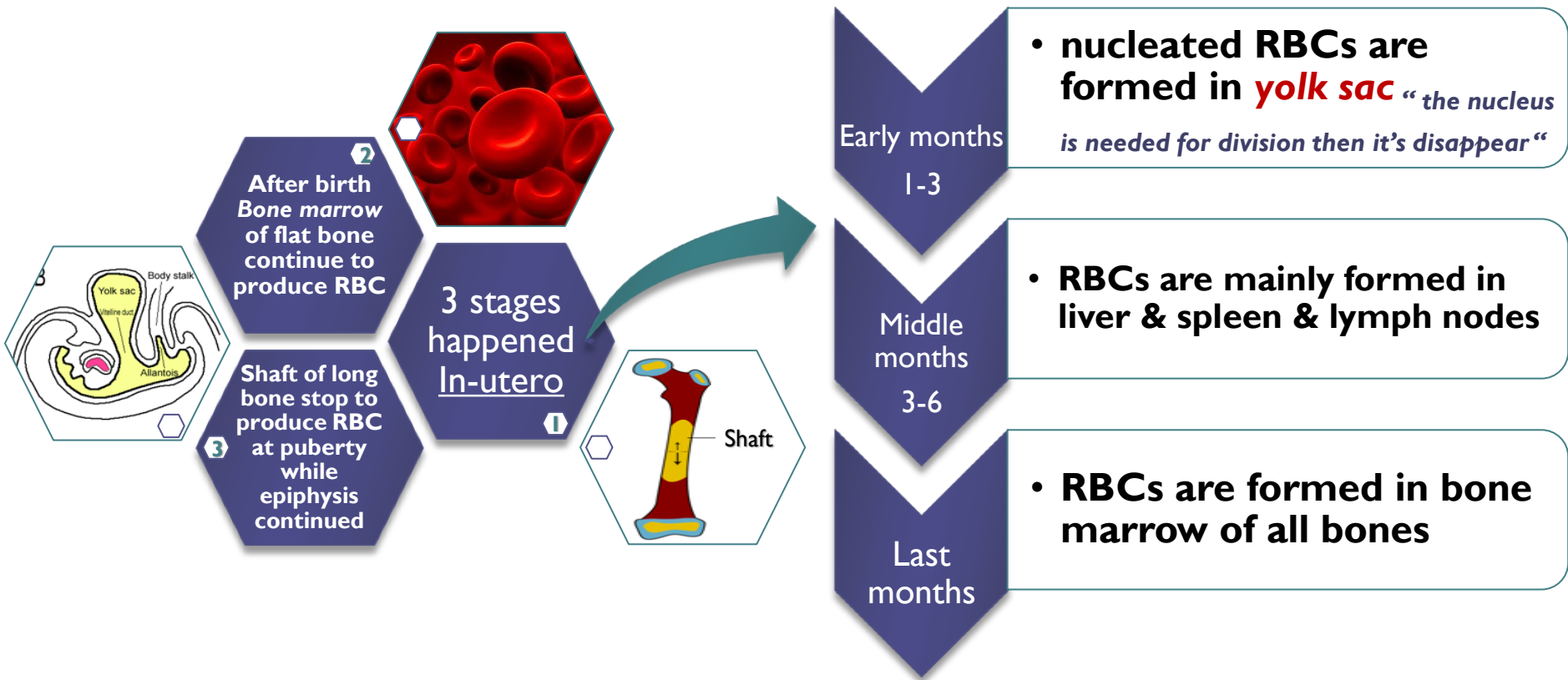
(**MCHC= 30 – 36 gm/dl**)

Microcytic Hypochromic Anemia	Macrocytic Normochromic Anemia	Microcytic hyperchromic Anemia
		
MCHC: <32 g/dL	MCHC: 32 – 36 g/dL	MCHC: >36 g/dL
Small sized RBCs with a large central pallor with concentration of hemoglobin decreased → Hence <b>reduced MCHC</b>	Big sized RBCs with a normal central pallor but concentration of hemoglobin remains → Hence <b>MCHC is normal</b>	Small sized RBCs with abnormal/without central pallor → increased hemoglobin concentration → hence <b>increased MCHC</b>

الجدول للإيضاح فقط

More explanation : [Vedio](#)

# Production of RBC



▶ ① **Permeability:**

Semipermeable membrane, gas and urea freely passing through.

▶ ② **Plasticity:** depends on:

- 1) surface area-cubage ratio
- 2) viscosity of Hb. “لزوجة”
- 3) membrane elasticity and viscosity.

▶ ③ **Osmotic fragility:**

Changes in RBC put into lower osmotic salty solution. Osmotic fragility of aged RBC is large and easily results in rupture (hemolysis and ghost cell).

Isosmotic solution : e.g. 0.85% NaCl & 1.4% NaHCO<sub>3</sub> , 5% glucose.

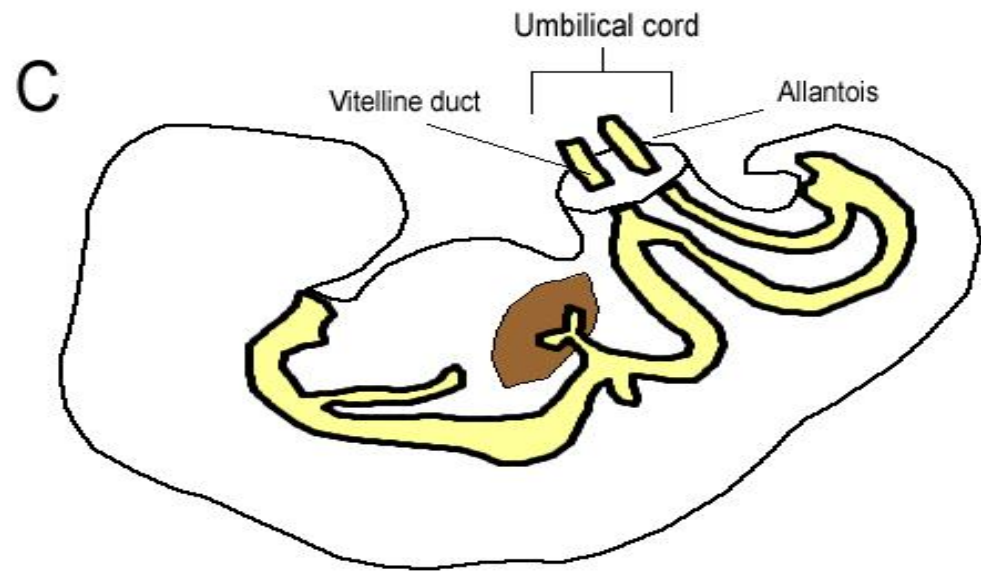
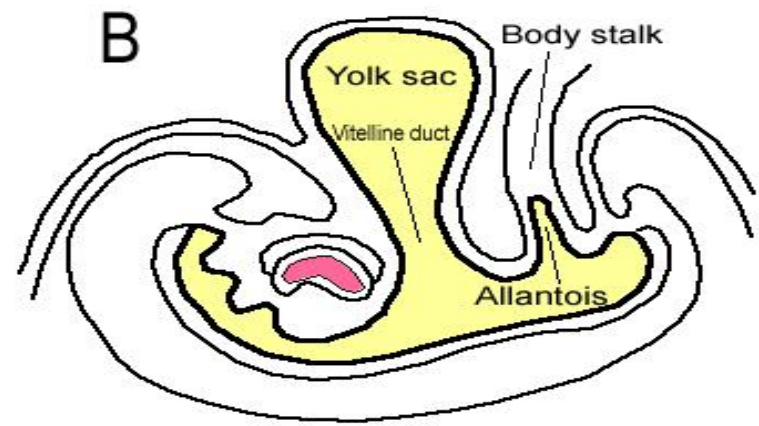
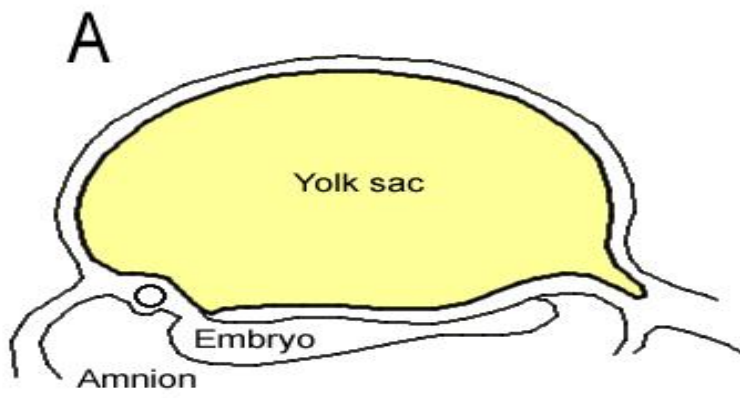
Isotonic solution : e.g. 0.85% NaCl.

▶ ④ **Suspension stability:**

it can be described by erythrocyte sedimentation rate (ESR) معدل الترسيب

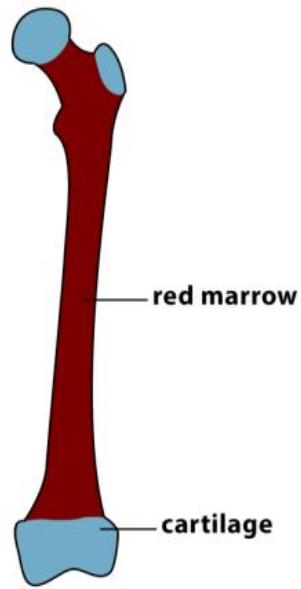
which is RBC descending distance per hour and suspension stability is inverse proportion to ESR.

Normal value : male : 0~15 mm/h / female : 0~20 mm/h.

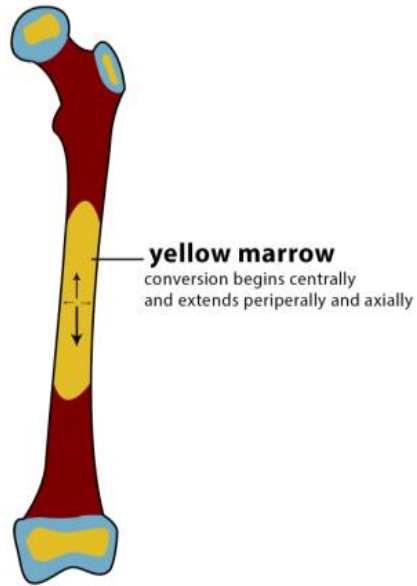


Production of RBC in utero

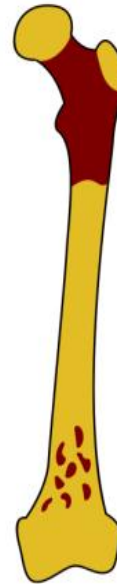




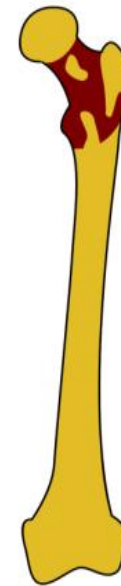
**Infant**  
<1 year



**Childhood**  
1-10 years



**Adolescent**  
10-20 years

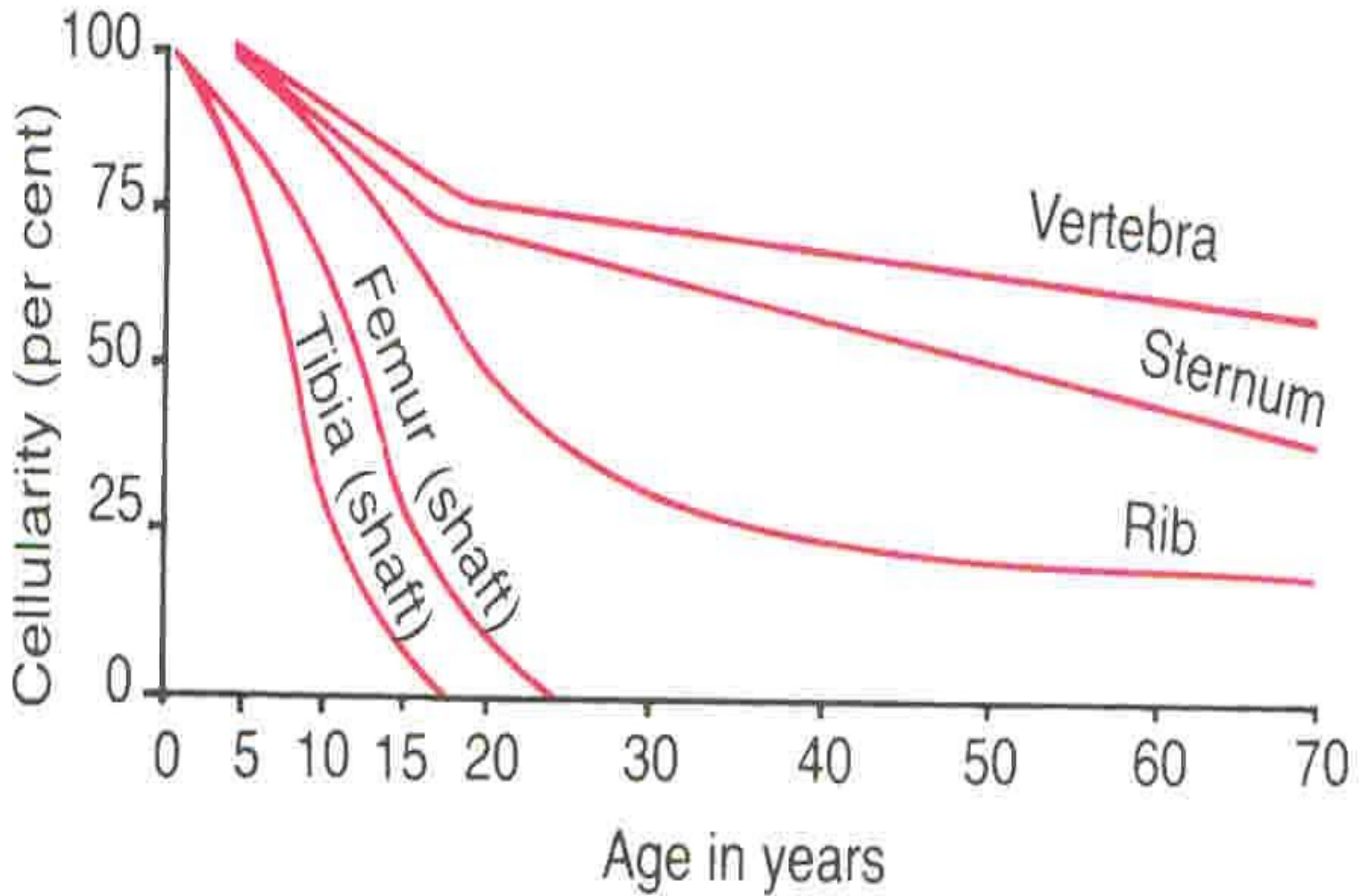


**Adult**  
>25 years

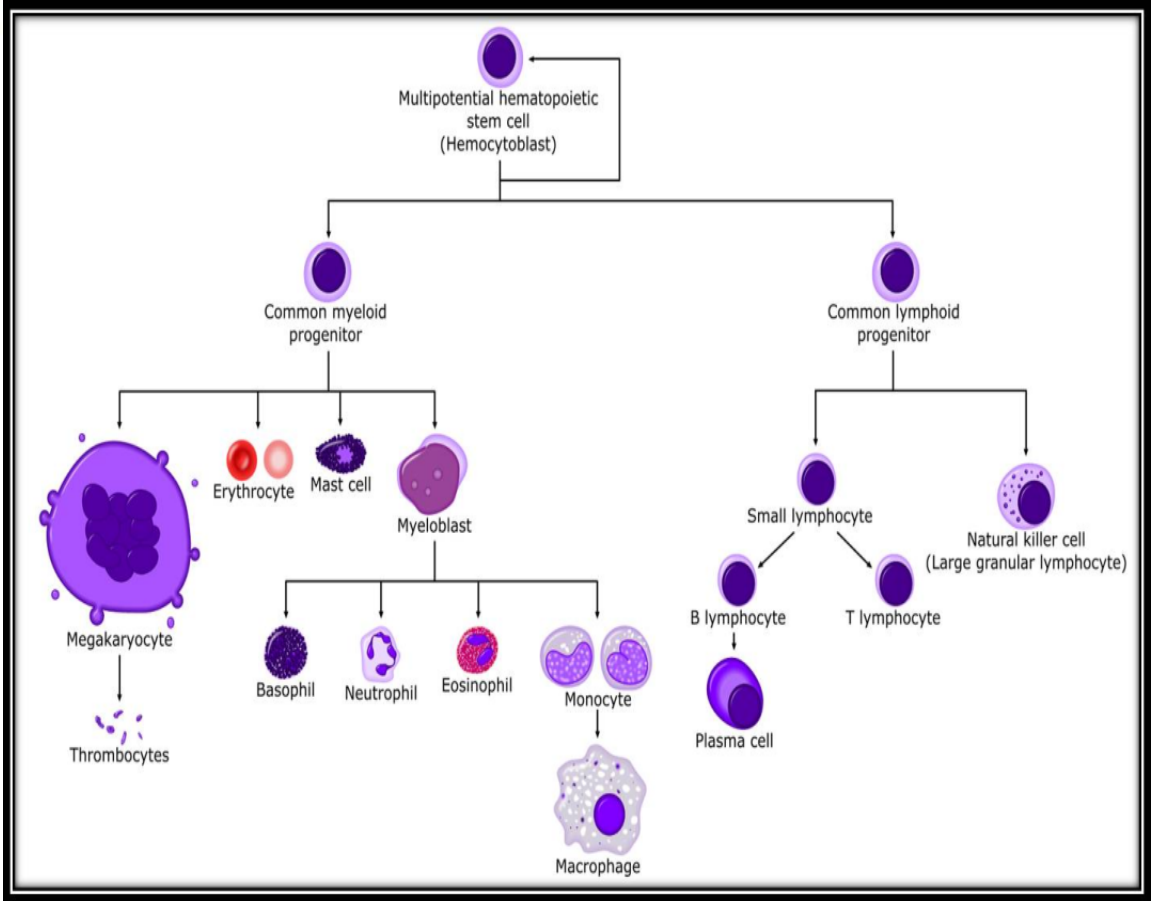


**Note:** Children need RBC more than adults for their growth





Production of RBCs in our life



شرح لمحتوى الصورة :

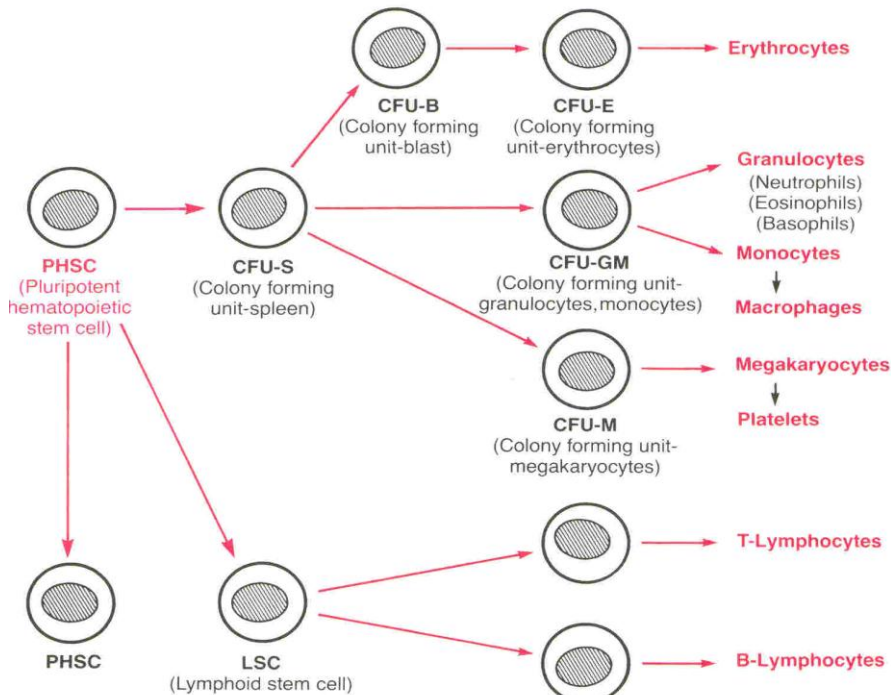
All blood cells are formed from ( **stem cells** ) > stem cell has two paths :

- One path is called “ **myeloid** “ ➔ that form ( RBCs ) + ( some type of WBCs ) + ( Platelets ) + ( mast cell )

- The other path is called “ **lymphoid** “ ➔ that formed (lymphocyte ) “ another type of WBC”

**Note:** stem cells can differentiate into a lot of different cells.  
- myeloblast gives white blood cells

# Genesis (Production) of RBC



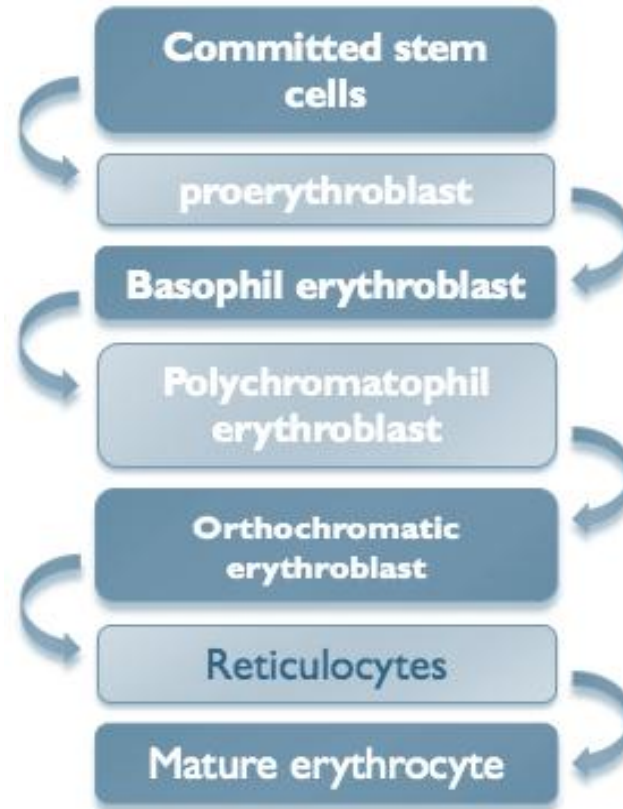
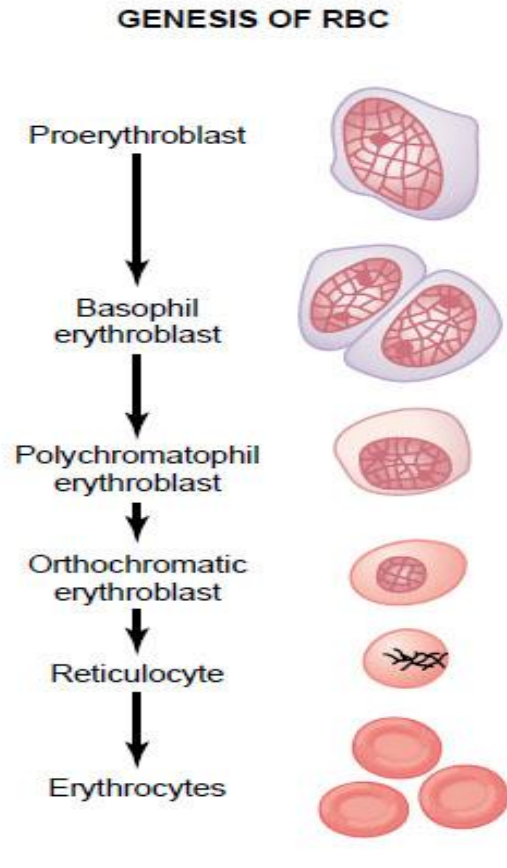
➤ **All blood cell are formed from Pluripotential hematopoietic stem cells ⇒ committed cells :**

- **Committed stem cells for RBC**
  - **Committed stem cells for WBC**
- **Growth of different stem cells are controlled by different growth factors.**

**Pluripotential hematopoietic stem cells : the cells that give rise to all the other blood cells.**

# Stages of differentiation of RBC

## Stages of RBC development :



**Note:** RBC goes into stages to get its concave structure  
reticulocyte is the stage where the cell loses its nucleus and is covered by a net.

# Erythropoiesis

**RBCs** development is characterize by :

In cases of rapid  
**RBC** production :  
Reticulocytes  
**increase** in the ↑  
circulation.

**Decrease** in cell  
size



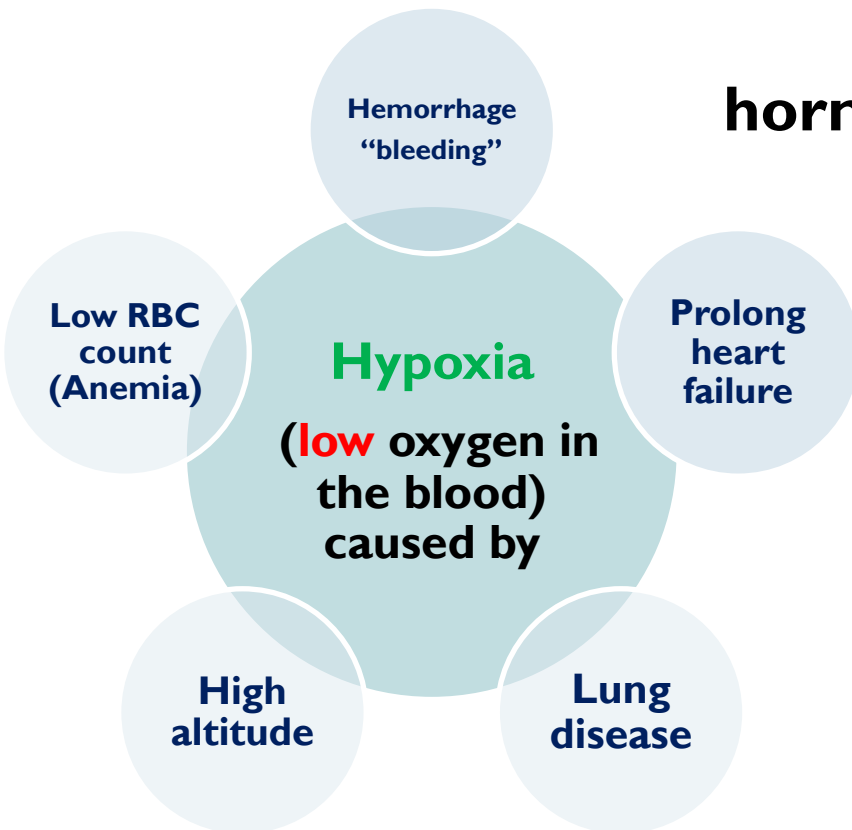
Disappearance  
of nucleus



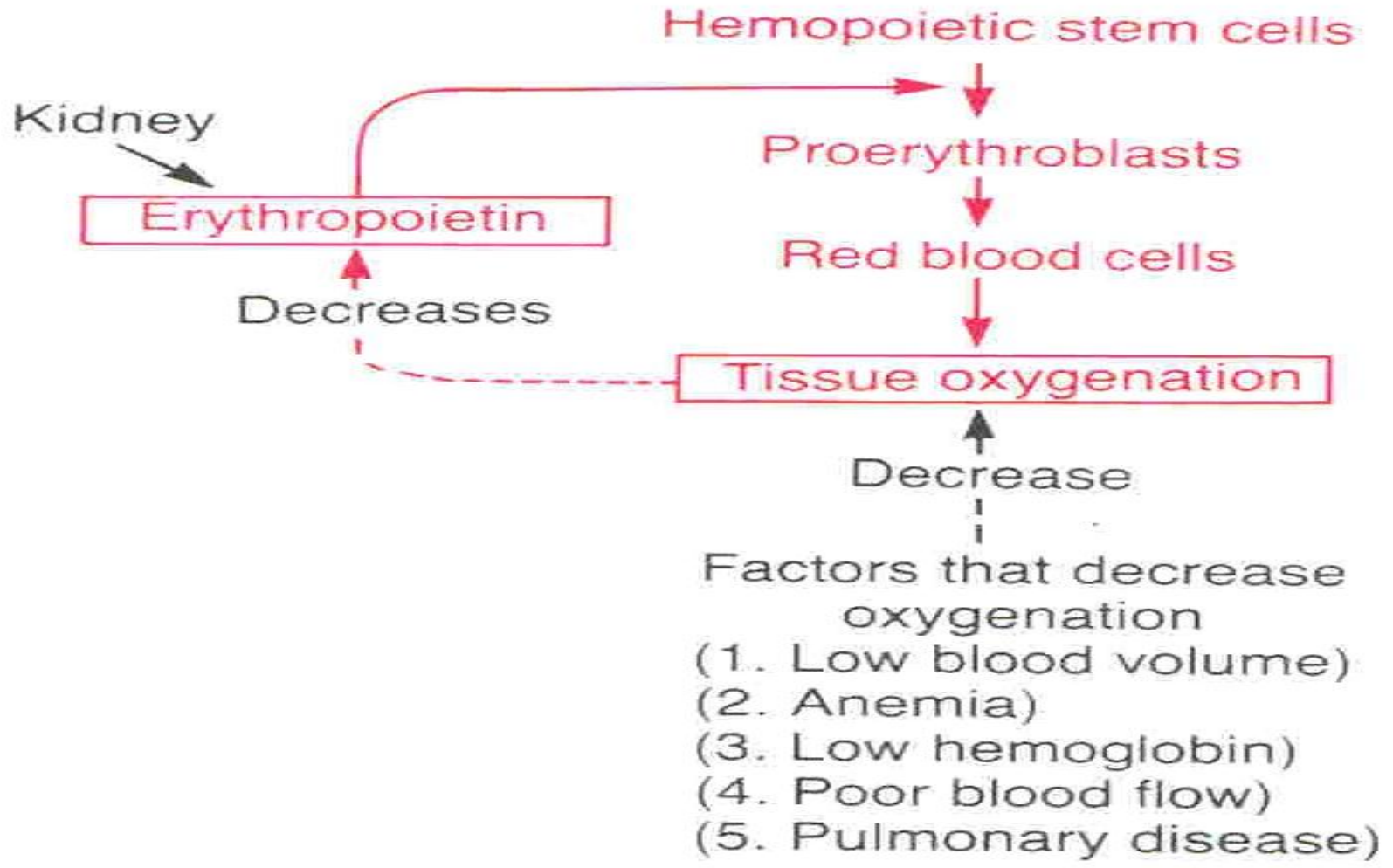
Appearance of  
hemoglobin  
(Hb)

# Erythropoiesis

▶ **Erythropoiesis** is stimulated by  
(**Erythropoietin**) which is:  
hormone produced by the kidney in  
response to Hypoxia

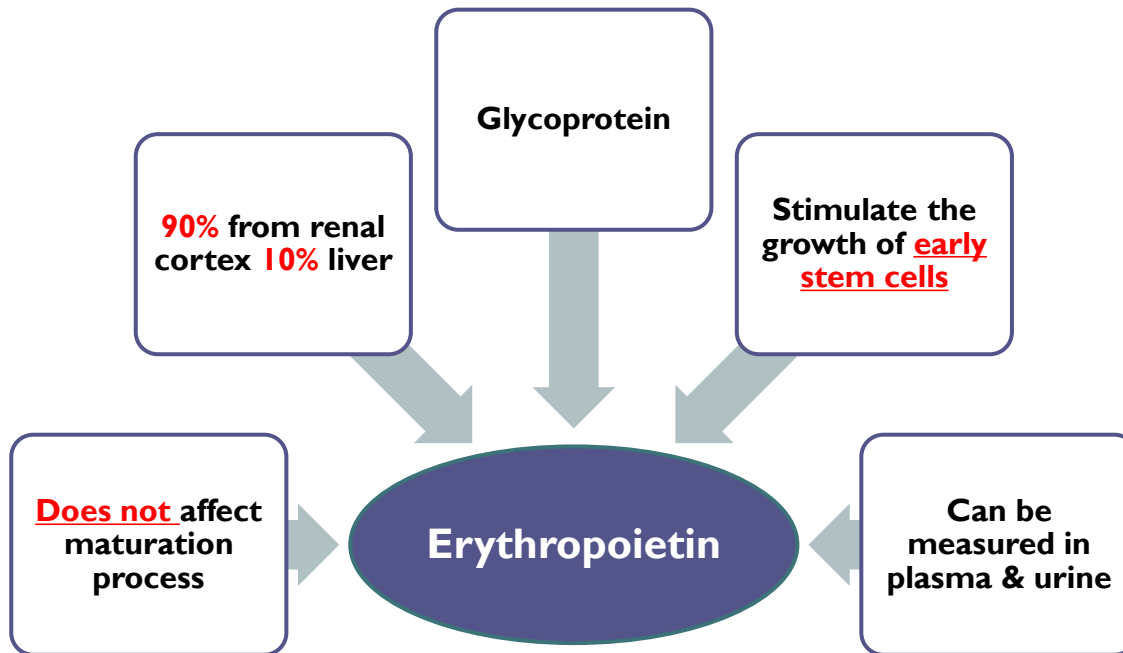








# Erythropoietin “ a hormone “



## Conditions like:

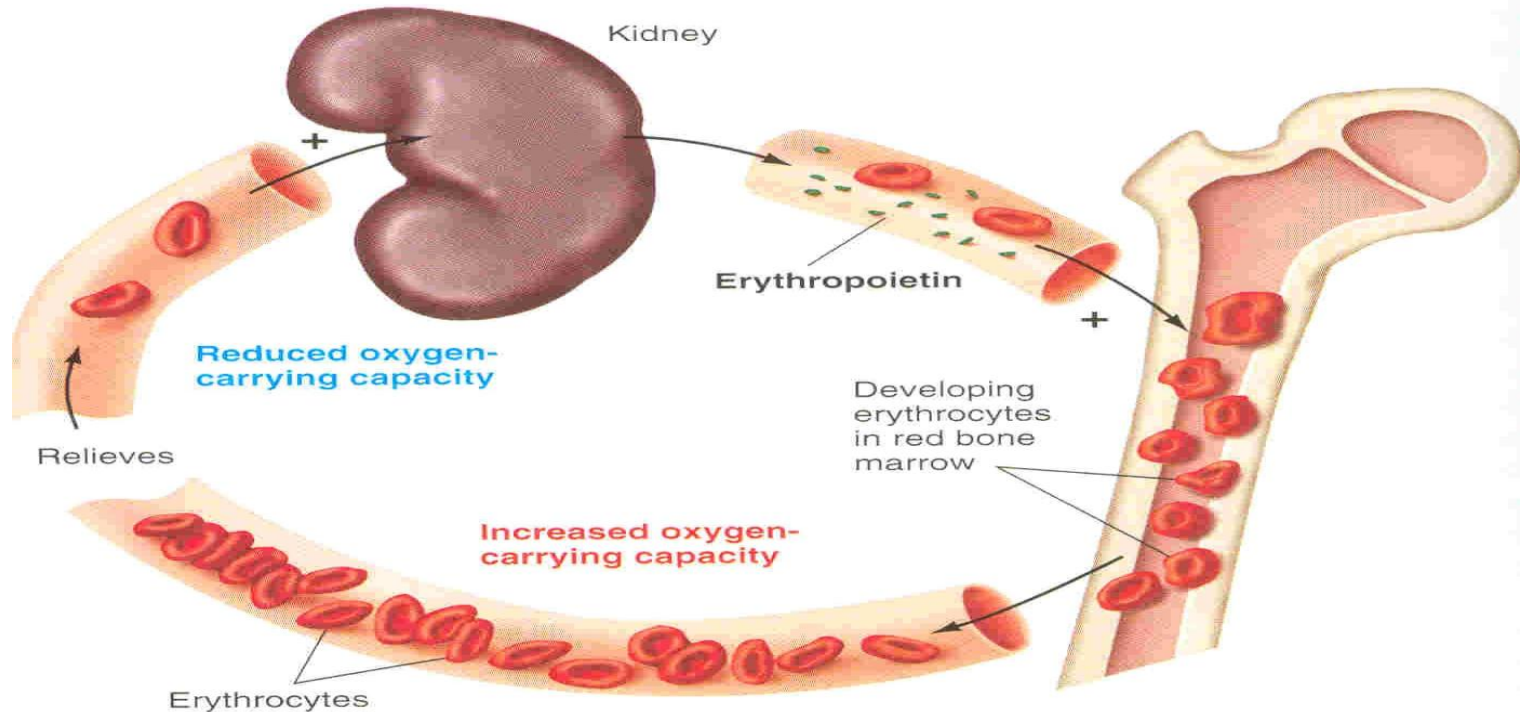
- Anemia.
- High altitude.
- Heart failure.
- Lung Disease.

Result in High erythropoietin levels and **polycythemia**

**Erythropoietin** is a protein control the early stages of ( red blood cells synthesis ), but not the meddle or last stages.

## Role of the kidneys in RBC formation

Kidney produces erythropoietin in response to hypoxia



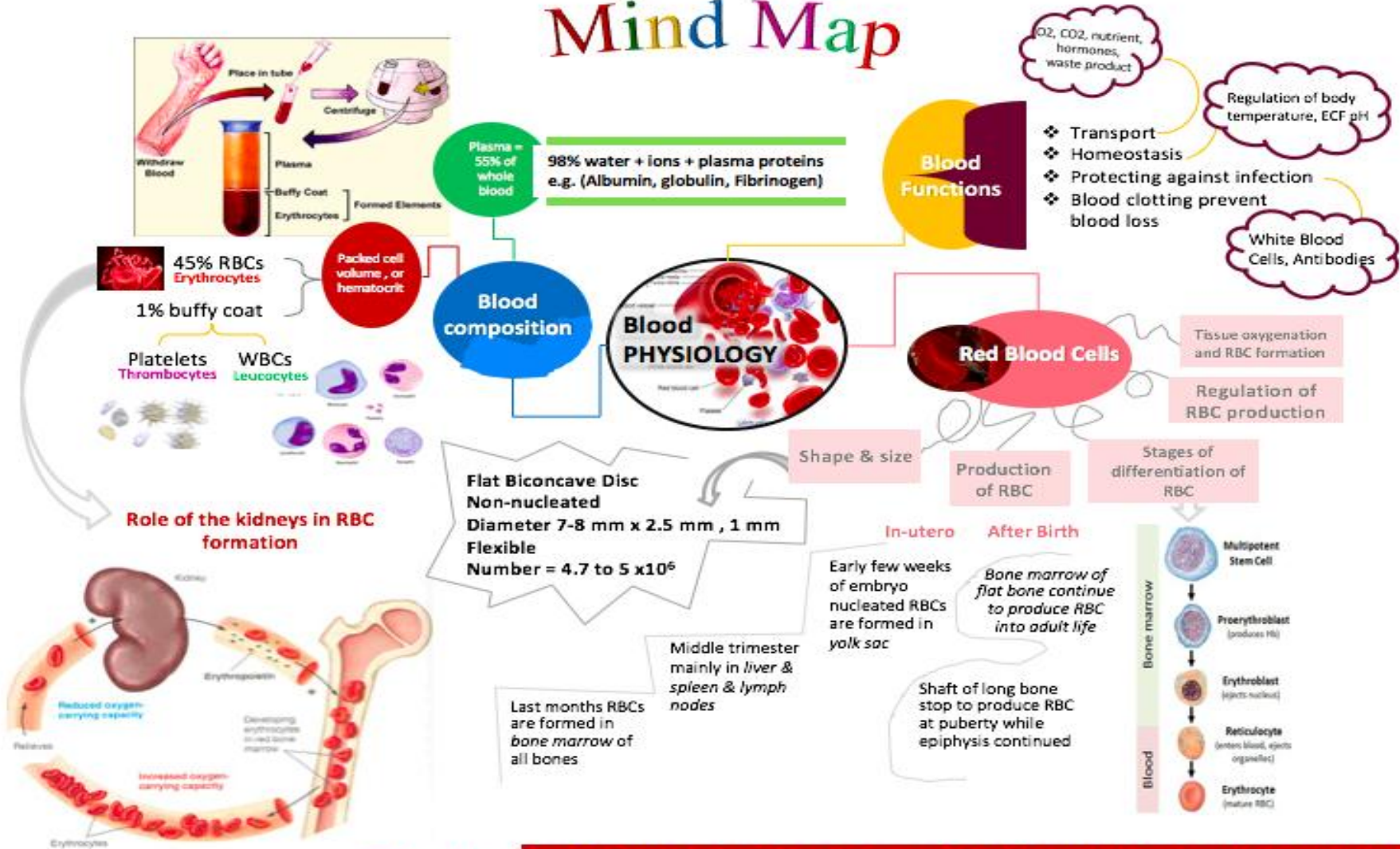
Healthy kidneys produce a hormone called erythropoietin and prompts the bone marrow to make red blood cells, which then carry oxygen throughout the body.

	<u>RBCs</u>	<u>WBCs</u>	<u>Platelets</u>
Organelles	Lack nuclei and mitochondria	Have nucleus and mitochondria	Lack nuclei
Shape	Flattened biconcave disc	granular and non-granular (amoeboid*)	Irregularly shaped (amoeboid*)
Size	Diameter: 7-8um	Differ in sizes according to types	Diameter : 2-3um
Movement	Flexible	Diapedesis can "slip between " capillary wall	_____
Life span	120 days	Differ in life span according to types	5-10 days

Has irregular shape and usually move freely in blood

# Summary

## Mind Map



**Note :** use this mind map for revision not studying cuz not all the info included !



9

## Blood physiology 2

- Very important
- Extra information
- Terms

( وَفِي أَنْفُسِكُمْ أَفَلَا تُبْصِرُونَ ) [سورة الذاريات الآية: ٢١]



# Objectives :

By the end of this lecture you should be able to:

- **Describe essential elements needed for RBC formation.**
- **Describe the process of Vit B12 absorption and its malabsorption.**
- **Recognize hemoglobin structure and its functions.**
- **Discuss iron metabolism (absorption, storage and transport).**
- **Describe the fate of old RBC.**
- **Describe anemia and its causes.**
- **Recognize causes of polycythemia.**

# Essential elements for RBCs formation and Maturation:

**Amino acids:**

Formation of **globin** in hemoglobin

sever protein deficiency  
→ **Anemia**

**Iron:**

Formation of hemoglobin

Deficiency → **Anemia**

**Vitamins:**

Vit B12 and Folic acid  
Synthesis of nucleoprotein

Deficiency → **Anemia**

Other :Vit B6,  
Riboflavin,  
nicotinic acid,  
biotin, Vit C, Vit E

**Hormones**

Androgens, Thyroid,  
cortisol & growth  
hormones

Deficiencies of any one  
results in **Anemia**

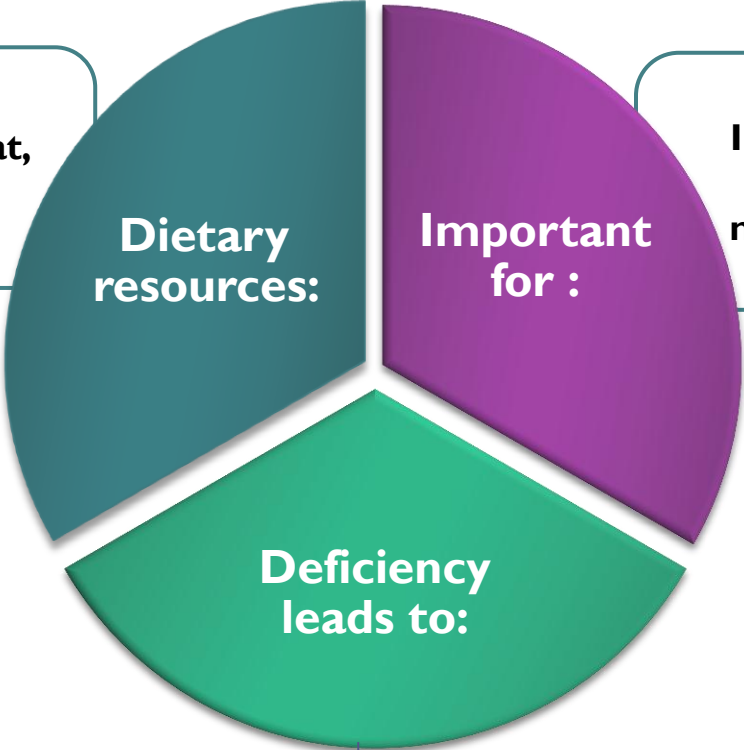
**Essential  
elements**

Copper, Cobalt, zinc,  
manganese

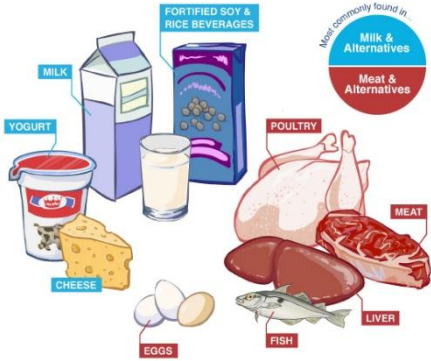


# Vitamin B12 & Folic acid

meat, milk, liver, fat,  
green vegetables.



Important for DNA  
synthesis and final  
maturation of RBC.



**Note:** macrocytic :  
the cell becomes  
big and it won't  
divide.

Failure of nuclear  
maturation &  
division

Abnormally large  
& oval shape RBC

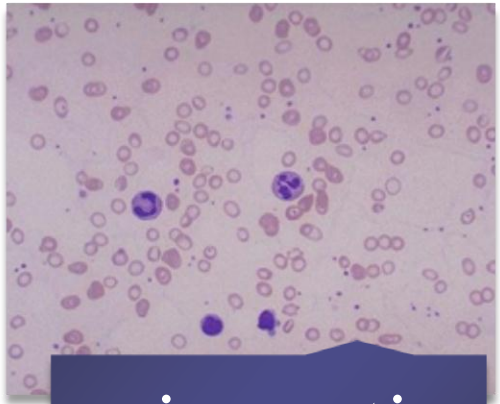
Short life  
span

reduced RBC  
count & Hb

Macrocytic  
(megaloblastic)  
anemia

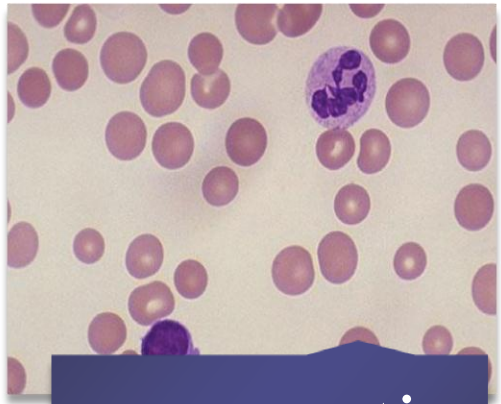
# Types of anemia

► Depends on the shape of the RBCs :



microcytic

The RBCs are **small** in size



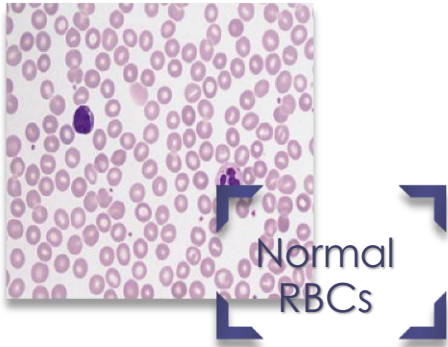
macrocytic

The RBCs are **large** in size



There's another type called : **Sickle anemia**  
Which the shape of RBCs change to a sickle خلايا الدم المنجلية

# Types of anemia



- There is also increased **anisocytosis** (variation in size) and **poikilocytosis** (variation in shape).

## microcytic

RBCs are **smaller** than normal

Have an increased zone of central pallor

**Hypochromic**  
(less hemoglobin in each RBC)

## Macrocytic

**Hyper** segmented neutrophil

RBCs are **larger** than normal  
RBCs are almost as large as the lymphocyte.

There are **fewer** RBCs

# Malabsorption of Vit.b12

Pernicious Anemia

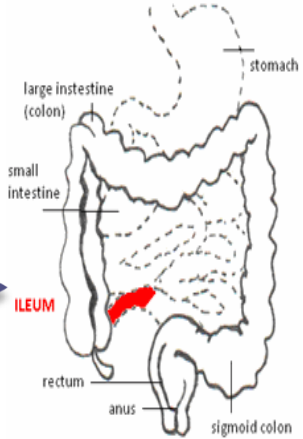
VBI2 absorption needs **intrinsic factor** secreted by parietal cells of stomach  
خلايا جدار المعدة

VBI2 + intrinsic factor is absorbed in the **terminal Ileum.**

Deficiency arise from (Causes of deficiencies):

Inadequate intake

Poor absorption due to **Intestinal disease**



Pernicious Anemia in a [video](#)

# Iron

Iron  
metabolism  
( Fe )

Iron  
Absorption  
( Fe )

total iron in the body = 4-5 g

65% hemoglobin

5% other hems

1% bound to transferrin  
(betaglobulin) in blood

15-30% stored iron in the form of  
ferritin in the liver, spleen and bone  
marrow

Iron is needed for  
the synthesis of  
hemoglobin,  
myoglobin  
cytochrome oxidase,  
peroxidase &  
catalase.

Iron in food mostly in oxidized  
form (Ferric ,  $F^{+3}$ )

Better absorbed in reduced  
form (Ferrous ,  $F^{+2}$  )

Iron in stomach is reduced by  
gastric acid, Vitamin C.

Rate of iron absorption depend  
on the amount of iron stored

- Iron is transport in plasma in the form of **Transferrin** (apotransferrin + iron)
- Iron is stored in two forms:
  - **Ferritin** (apoferritin + iron)
  - **Hemosiderin** (insoluble complex molecule, in liver, spleen, bone marrow)
- Daily loss of iron is **0.6 mg in male & 1.3 mg/day in females**

Transferrin in a [video](#)

# Destruction of RBC

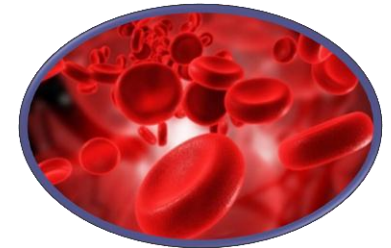
RBC life span in circulation = **120** days

Metabolic active cells

Old cell has a fragile cell membrane, cell will rupture as it passes in narrow capillaries and spleen

Released **Hb** is taken up by macrophages in liver, spleen & bone marrow:

**Hb** is broken into its component:



-Polypeptide —amino acids  
(protein pool = storage)  
-Iron ---- ferritin  
-Haem (Porphyrin) →  
bilirubin → secreted by the liver into bile.  
[excess destruction of RBC Jaundice]



▶ **Definition :**

- Decrease number of RBC.
- Decrease Hb (Hemoglobin).

▶ **Symptoms :**

- Tired , Fatigue , short of breath and heart failure.

Normal Amount  
of red blood cells



Anemic Amount  
of red blood cells



# Causes of anemia

## Blood Loss

- **Acute** : ➡ accident  
(RBC return to normal 3-6 w)
- **Chronic** : ➡ microcytic hypochromic anemia (ulcer, worms)

## Decrease RBC production

- **Nutritional causes** :
  - Iron : ➡ microcytic Hypochromic anemia
  - Vit B12 & Folic acid : ➡ megaloblastic anemia .
- **Bone marrow failure** :  
destruction by cancer, radiation, drugs Aplastic anemia.

## Hemolytic (Excessive destruction)

- **Abnormal cells or Hb** :
  1. Spherocytosis
  2. sickle cells
- **Incompatible blood transfusion.**
- **Erythroblastosis fetalis**

# Polycythemia

## Result

Increased  
number  
of **RBCs**

## Types

### 1. Primary :

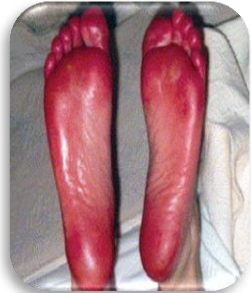
( **Polycythemia Rubra Vera – PRV** ):

uncontrolled RBC  
Production. [video](#)

### 2. Secondary :

to **hypoxia** : high  
altitude(physiological),  
chronic respiratory or  
cardiac disease

[video](#)

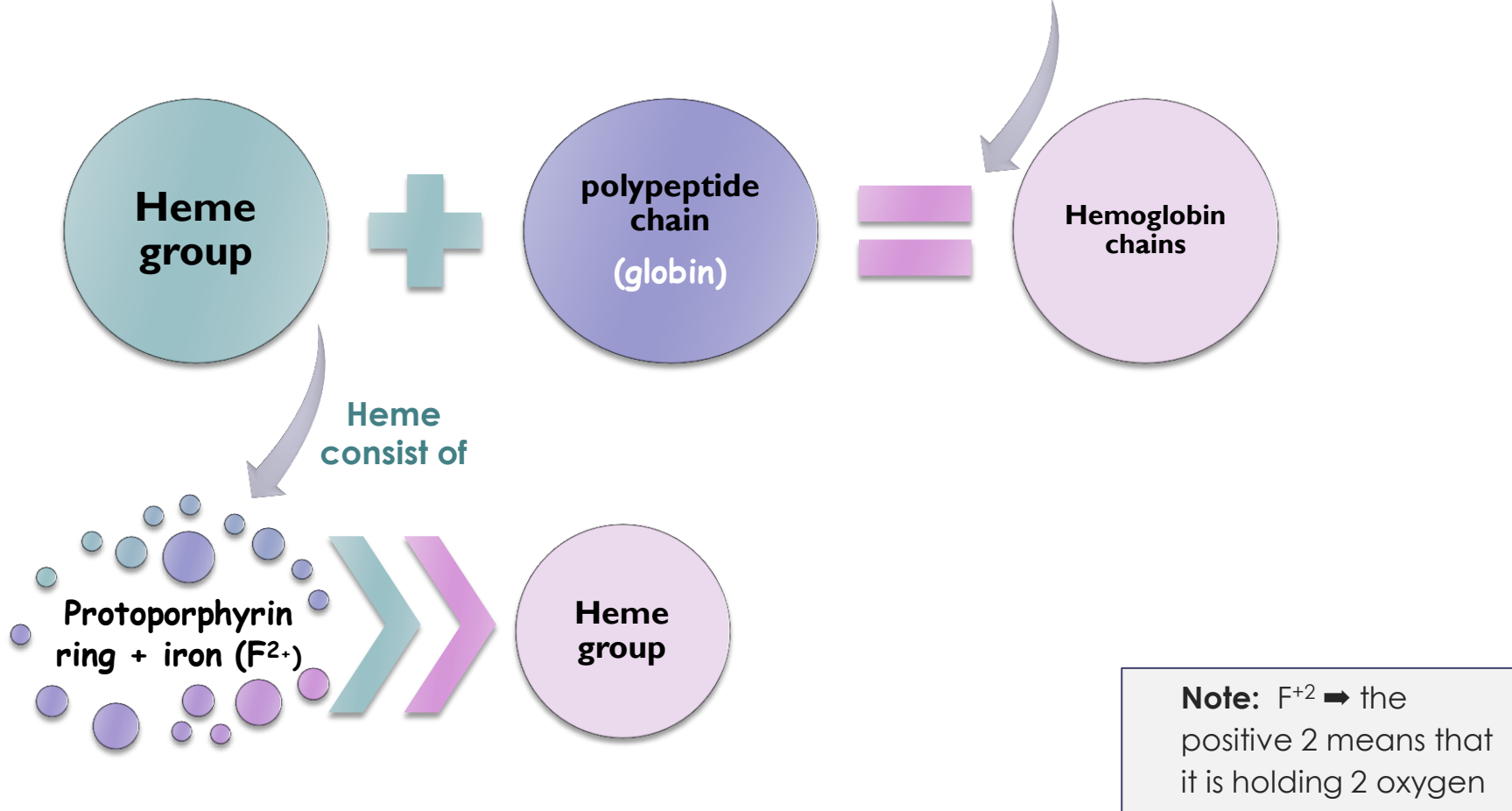


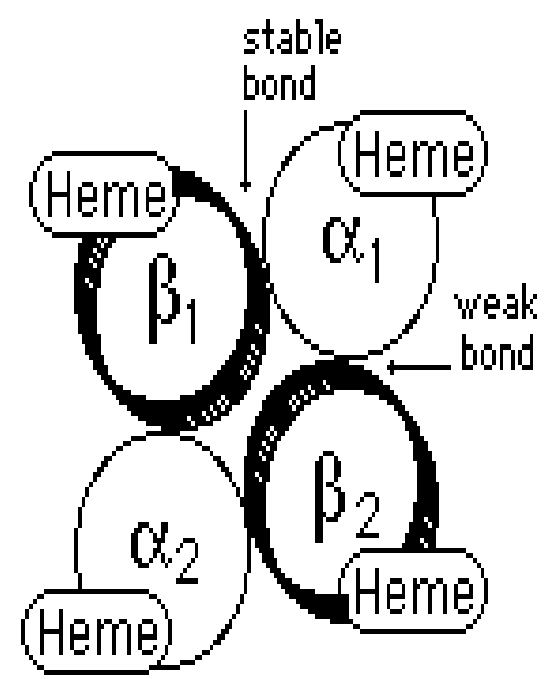
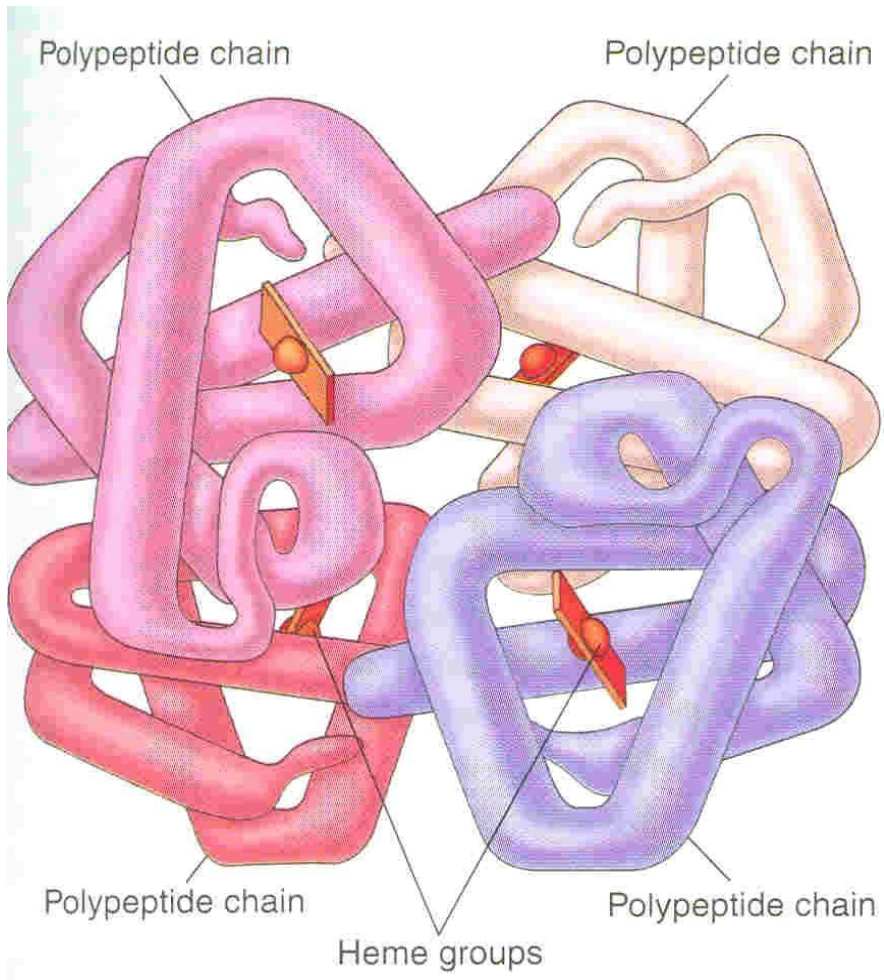
**Note:** primary: unknown reason

- **Polycythemia** : increase in RBCS , while **Anemia** is decreased in RBCs

# Structure of HAEMOGLOBIN

► Hb molecules consist 4 chains each chain formed of





**Structure of hemoglobin**

# Types of HB

## Normal

**Hb A** (2 alpha  
& 2 beta chains)  
(adult Hb)  
(98%).

**Hb A2** (2 alpha & 2  
delta chains)  
(2%)

**Hb F** (2 alpha & 2  $\gamma$   
"gamma" chains)  
(Hb of intrauterine life).

## Abnormal

Abnormality in  
the polypeptide  
chain

abnormal Hb  
(Hemoglobinopathies)

e.g. thalassemia,  
sickle cell (HBS).

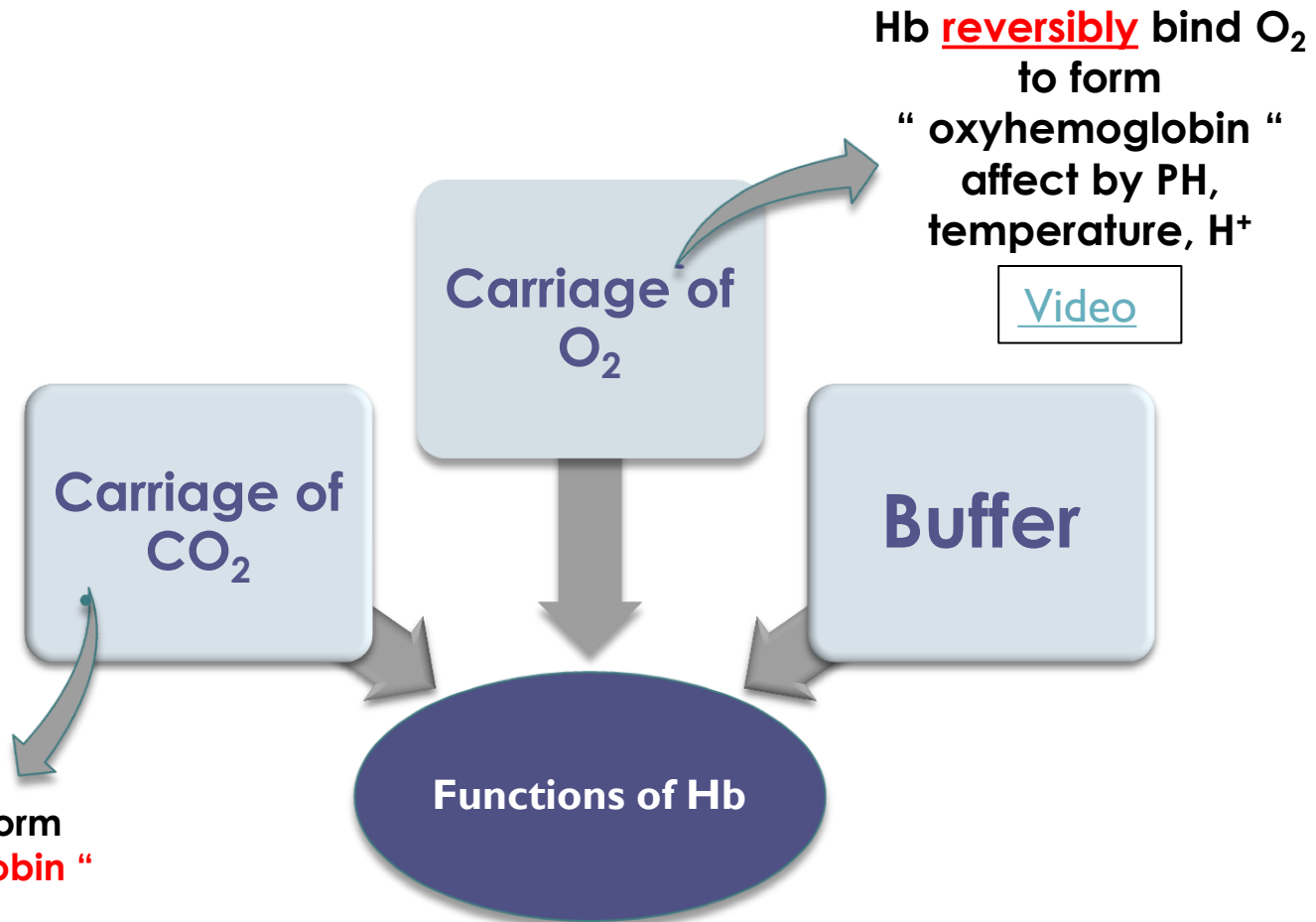
**Thalassemia :**  
[video1](#) , [video2](#)  
[Types of Hb](#)

**Note:** Hb F has high affinity to oxygen than Hb A





# Functions of hemoglobin



Check your understanding : [Quiz](#)

## Videos :

[Red blood cell life cycle](#)

[How are Red Blood Cells made? Erythropoiesis - Erythropoietin – Regulation](#)

[Anemia](#)

[Macrocytic Anemia & Microcytic Anemia](#)

[Hemoglobin Structure](#)

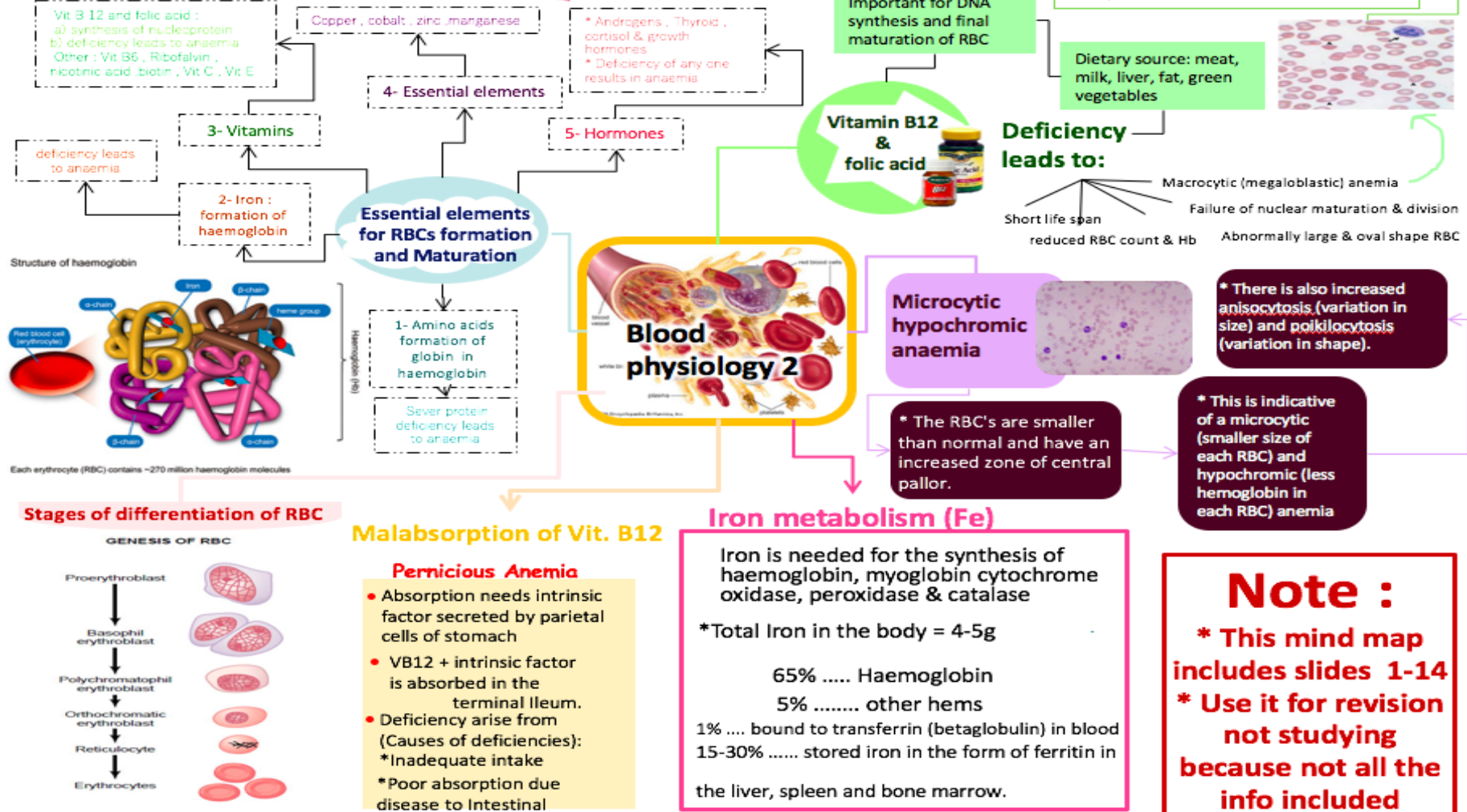


التبرع بالدم ينشط خلايا نخاع العظم للمتبرع مما يزيد فاعليتها ويجدد نشاطها فتنتج المزيد من خلايا الدم الجديدة فيبينما يتجدد دم الإنسان كل ١٢٠ يوم فإن دم المتبرع يتجدد كل ٢٠ يوم !

# Summary

A

## Mind Map



# Summary

B

## Mind Map

**Note :** \* This mind map includes slides 15-25  
\* Use it for revision because not all the info is included

### Iron absorption

Iron in food mostly in **oxidized** form (Ferric, F+3)  
**Better absorbed** in reduced form (Ferrous, F+2)

Iron in stomach is **reduced** by gastric acid, Vitamin C

Rate of iron **absorption** depend on the amount of iron **stored**

Iron is transport in plasma in the form of **Transferrin (apotransferrin + iron)**

### Transport and storage of iron

Iron is stored in two forms

- \* Ferritin (apoferritin + iron)
- \* Hemosiderin (insoluble complex molecule, in liver, spleen, bone marrow)
- \* Daily loss of iron is 0.6 mg in male & 1.3mg/day in females.

### Destruction of RBC

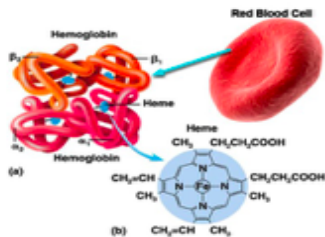
- RBC life span in circulation = **120 days**.
- Metabolic active cells.
- Old cell has a fragile cell membrane, cell will rupture as it passes in narrow capillaries (and spleen).
- Released Hb is taken up by macrophages in liver, spleen & bone marrow:  
**Hb is broken into its component**
- Polypeptide—amino acids (protein pool = storage)
- Iron ---- ferritin

Haem (Porphyrin) → bilirubin → secreted by the liver into bile. [excess destruction of RBC jaundice]



### Blood physiology 2

### ) Polycythemia (Increased number of RBC



compositions  
Types  
functions

### Haemoglobin

### 3. Haemolytic → excessive destruction    2. Decrease RBC production    1. Blood Loss

Causes of anaemia

### ANAEMIAS

#### Definition

Decrease number of RBC  
Decrease Hb

#### Symptoms:

Tired, Fatigue, short of breath, heart failure

#### Nutritional causes

Iron → microcytic hypochromic anaemia.  
Vit B12 & Folic acid → megaloblastic anaemia

Bone marrow failure:  
destruction by cancer, radiation, drugs Aplastic anaemia

a. Acute  
accident (RBC return to normal 3-6w)

b. Chronic  
microcytic hypochromic anaemia (ulcer, worms)

- Abnormal cells or Hb
  - Spherocytosis
  - sickle cells
- Incompatible blood transfusion.
- Erythroblastosis fetalis .



## Physiology team

عمر العتيبي  
رواف الرواف  
حسن البلادي  
عمر الشهري  
عادل الشهري  
عبدالله الجعفر  
عبدالرحمن البركة  
محمد الشيباني  
خليل الدريبي  
عبدالعزیز الحماد  
عبدالعزیز الغنايم  
عبدالمجيد العتيبي

خولة العماري  
الهونف الجلعود  
إلهام الزهراني  
رغد النفيسة  
نورة القحطاني  
منيرة الحسيني  
منيرة السلولي  
ريم البهلال  
عريب العقيل  
ملاك الشريف  
منيال باوزير  
فتون الصالح  
أفنان المالكي  
ربي السليمي