Erythropoiesis

Editing file

Color index:

- Main Text
- IMPORTANT
- Girls' slides only
- Boys' slides only
- Extra Info
- Drs Notes

Objectives:

1- Define Erythropoiesis; leucopoiesis; thrombopoiesis.

2-Recognize sites of RBC formation at different developmental age.

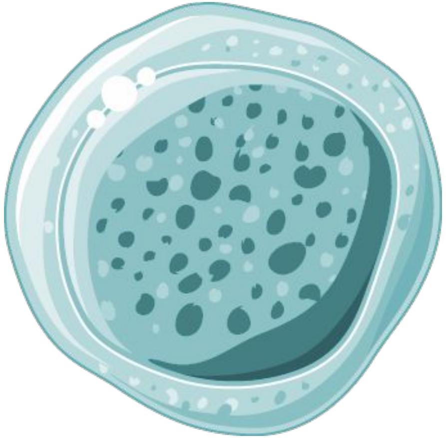
3- Describe different stages of RBC differentiation.

4- Describe features of RBC maturation.

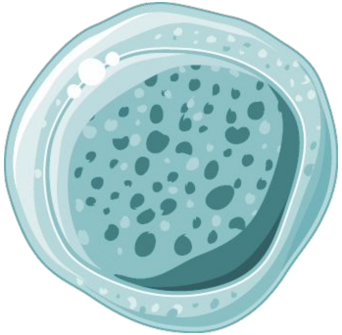
5- Describe regulation of RBC production & erythropoietin hormone secretion in response to Hypoxia.

6- Recognize clinical conditions associated with high level of erythropoietin in the blood.

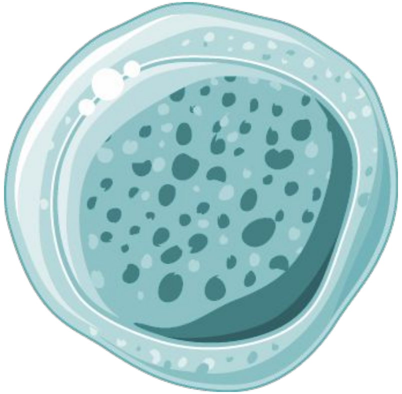
Blood Cells Formation



Erythropoiesis:
Formation of RBC (erythrocytes)



Leucopoiesis:
Formation of WBC (leucocytes)



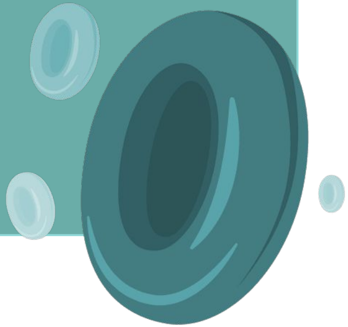
Thrombopoiesis:
Formation of platelets (thrombocytes)

Erythro = red
Leuco = white
Poiesis = formation

Red Blood Cells (RBC):

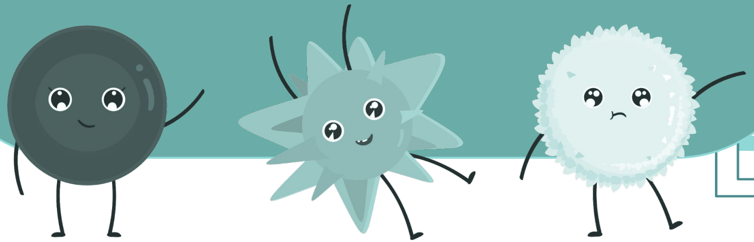
Function:

- O_2 transport
- CO_2 transport
- Buffer

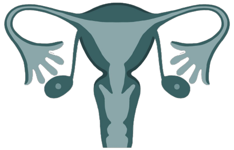


Shape & size

- Flat Biconcave Disc.
- Non-nucleated. (we need space for Hb)
- Diameter 7-8
- Flexible (to enter the capillaries)
- Average volume 90-95 μm3
- Number = 4.7 - 5 x106
- Hb = 14-16 g/dl



Production of RBC

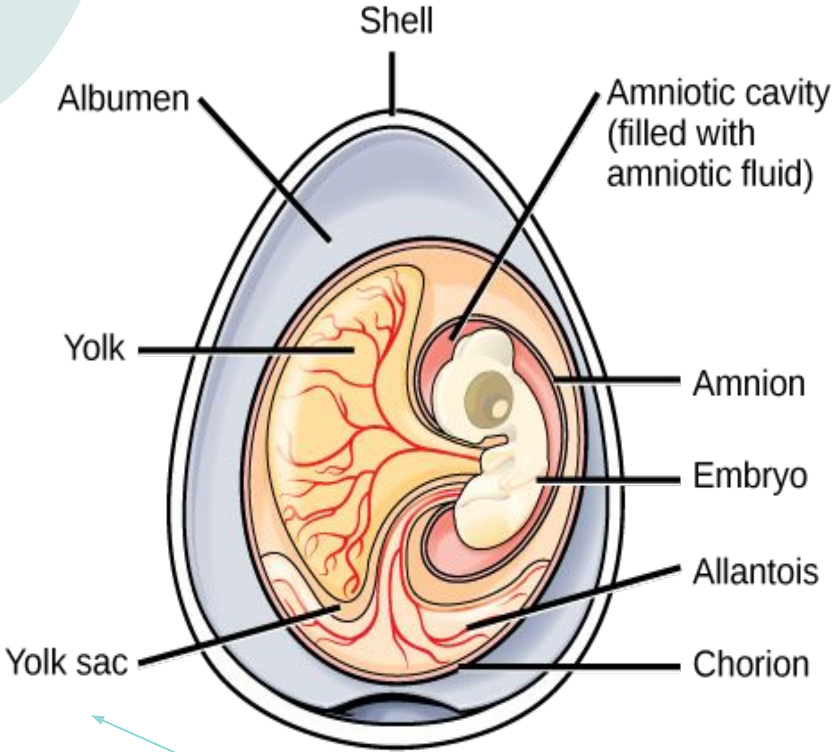


In-utero:

1. Early few weeks (first 3 months) of embryo nucleated RBCs are formed in yolk sac.
2. Middle trimester (3-6) mainly in liver & spleen & lymph nodes
3. Last months (6-9) RBCs are formed in bone marrow of all bones

After Birth:

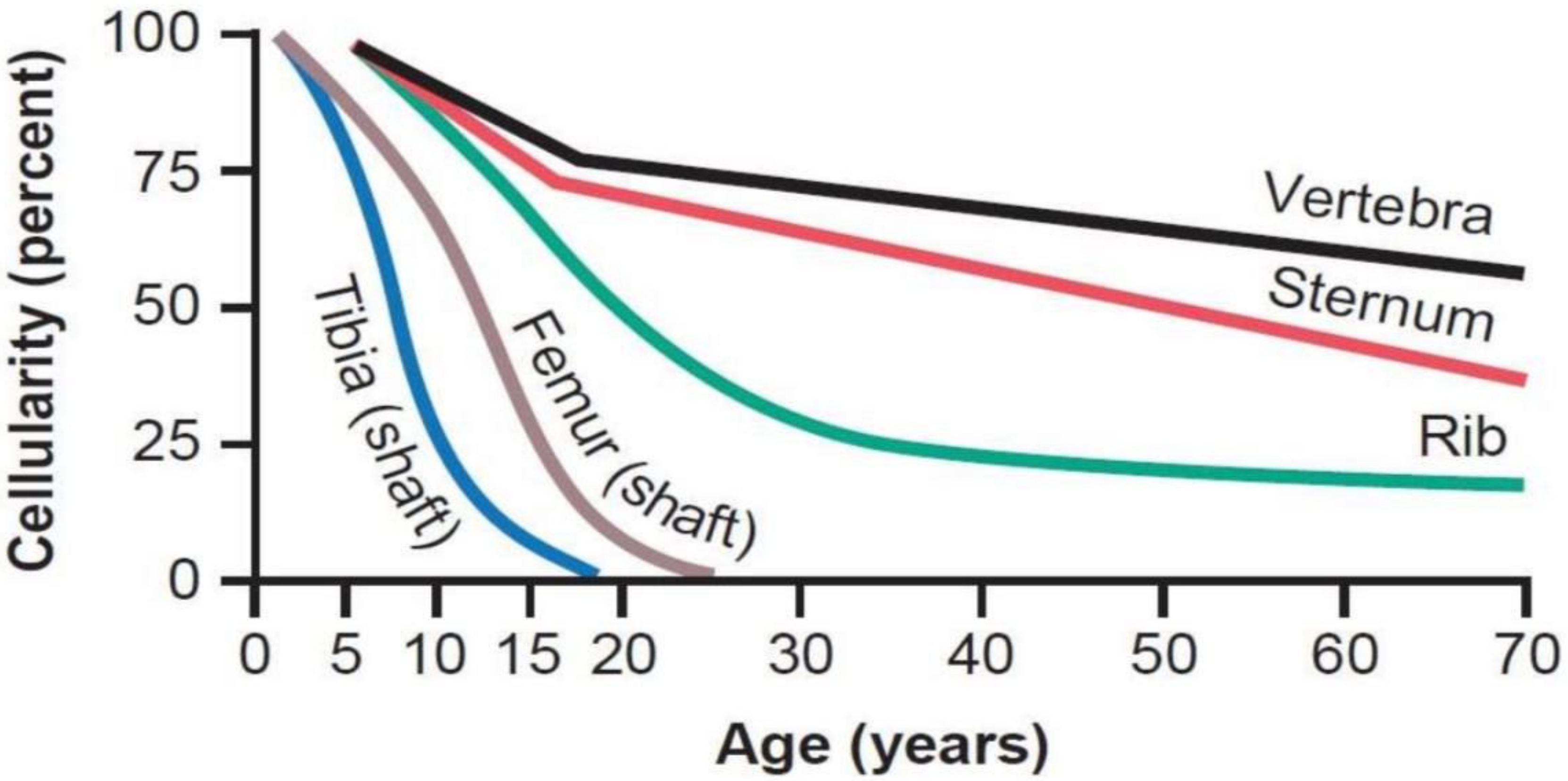
1. Bone marrow of flat bone continue to produce RBC into adult life.
2. Shaft of long bone stop to produce RBC at puberty while epiphysis continue.



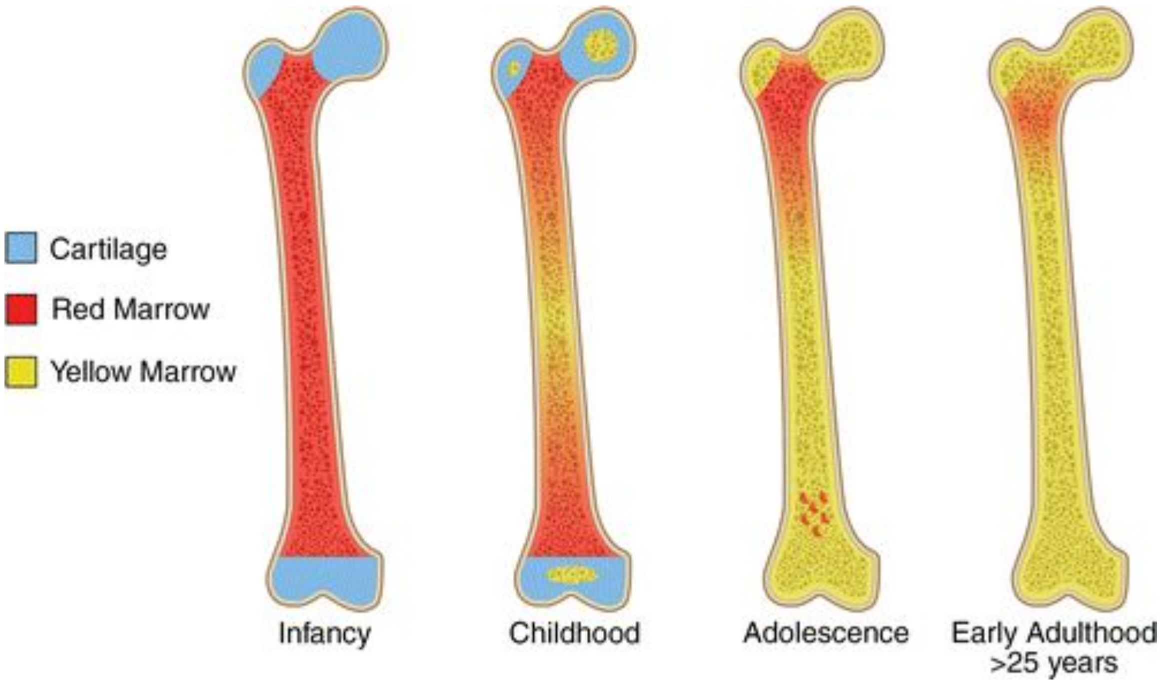
Bone marrow is disappeared from some places

Because of growth bone marrow is found everywhere

RBCs Erythropoiesis Sites



normal bone marrow conversion



Pluripotent Stem Cells in Bone Marrow & Cord Blood

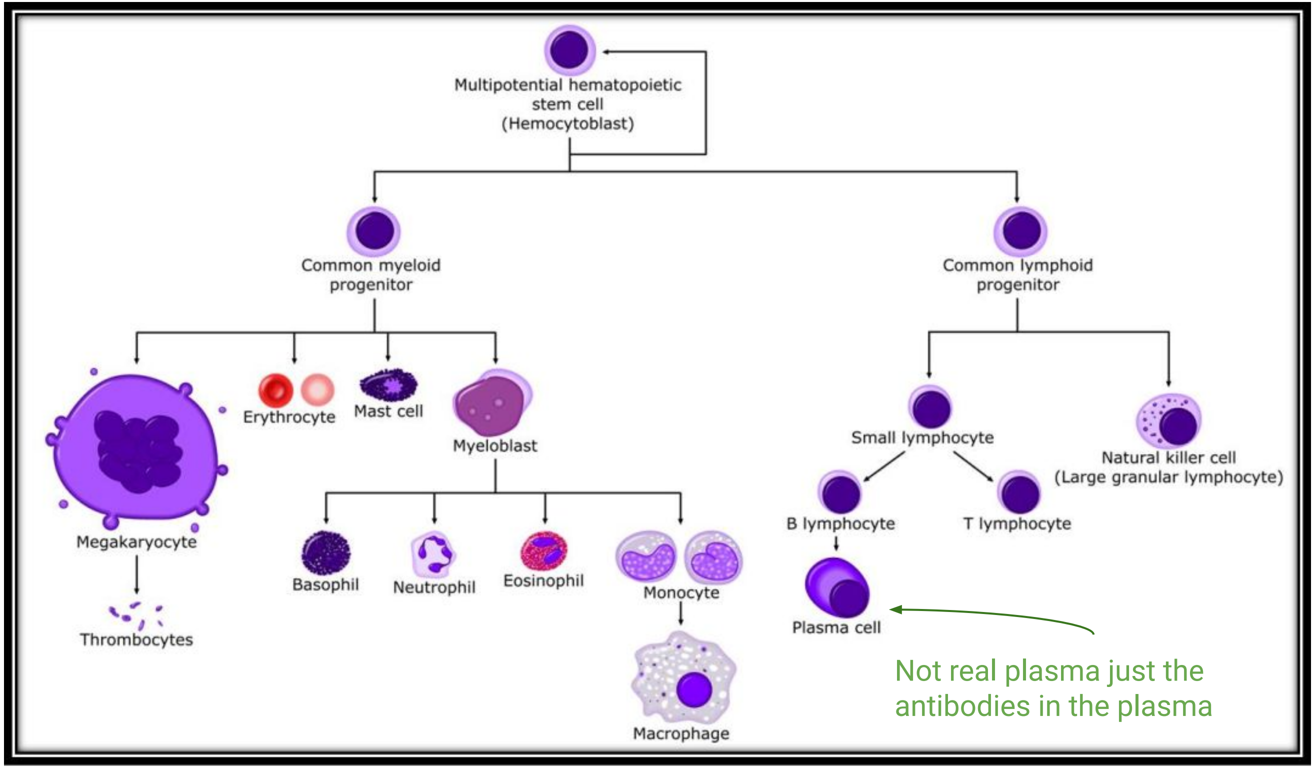


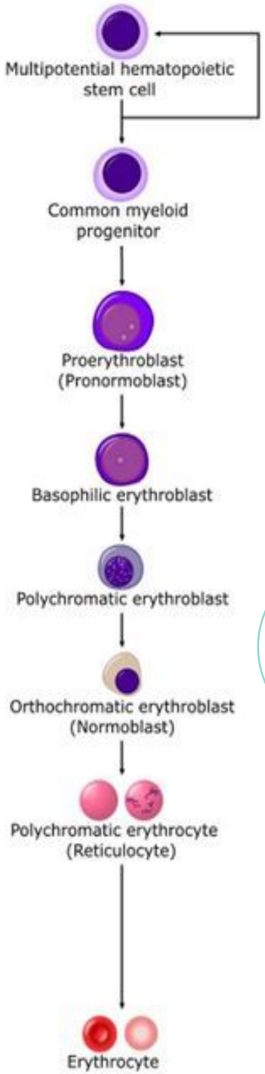
Figure 1: Hematopoiesis in Bone Marrow

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.

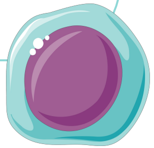
❖ Growth of different stems cells are controlled by different growth factors. (هذي المعلومة هي زبدة الصورة الي قبل)



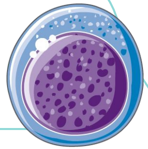
Stages of RBC development and differentiation:

(محتمل تجي ساك)

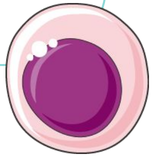
Committed stem cell



Proerthroblast



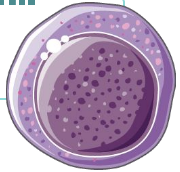
basophil erythroblast



(لونها أزرق)

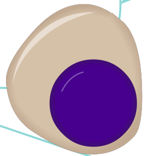
(حجمها يقل والنوية تبدأ تختفي)

polychromatophil erythroblast



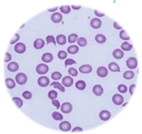
(متعددة الألوان)

Orthochromatic erythroblast



(لون واحد)

Reticulocytes



(فيها شبكة)

Mature erythrocytes

RBCs Erythropoiesis Factors

Oxygen supply to the tissues (Hypoxia).

Dietary requirements (Vitamins – Iron – Copper – Cobalt – Zinc – Other elements)

Healthy organs:
-Bone marrow
-Liver
- Kidney

Hormones (Erythropoietin – Androgens – Thyroxin – Cortisol)

- Boys' slides only

Erythropoiesis

*In cases of rapid RBC production: it will increase reticulocytes in the circulation. (normal reticulocytes percentage is 2%)

RBC development is characterized by:

- Decrease in cell size.
- Disappearance of nucleus.
- Appearance of hemoglobin (Hb)

Causes of Decreased Oxygen supply to the tissues (Hypoxia):

- High Altitudes
- Hematological disorders
- Cardiac or respiratory diseases.**(Prolong heart failure and lung disease)**
- Defective tissue utilization(e.g.Drugs & Toxins)
- Relative deficiency(increased demands as in athletes)
- Stagnation of blood flow (Thrombosis or Embolism)
- **Low RBC count (Anaemia)**
- Hemorrhage

Erythropoiesis is stimulated by erythropoietin hormone produced by the kidney in response to hypoxia (low oxygen in the blood)

Erythropoietin:

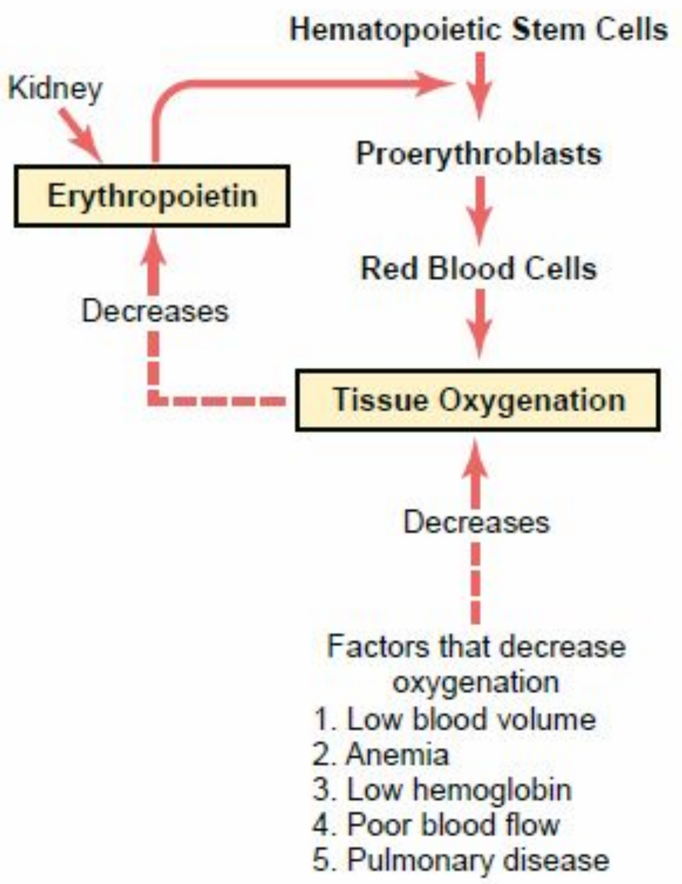
- Glycoprotein.
- 90% from renal cortex 10% liver. Stimulate the growth of early stem cells.
- Does not affect maturation process.
- Can be measured in plasma & urine.

conditions like:

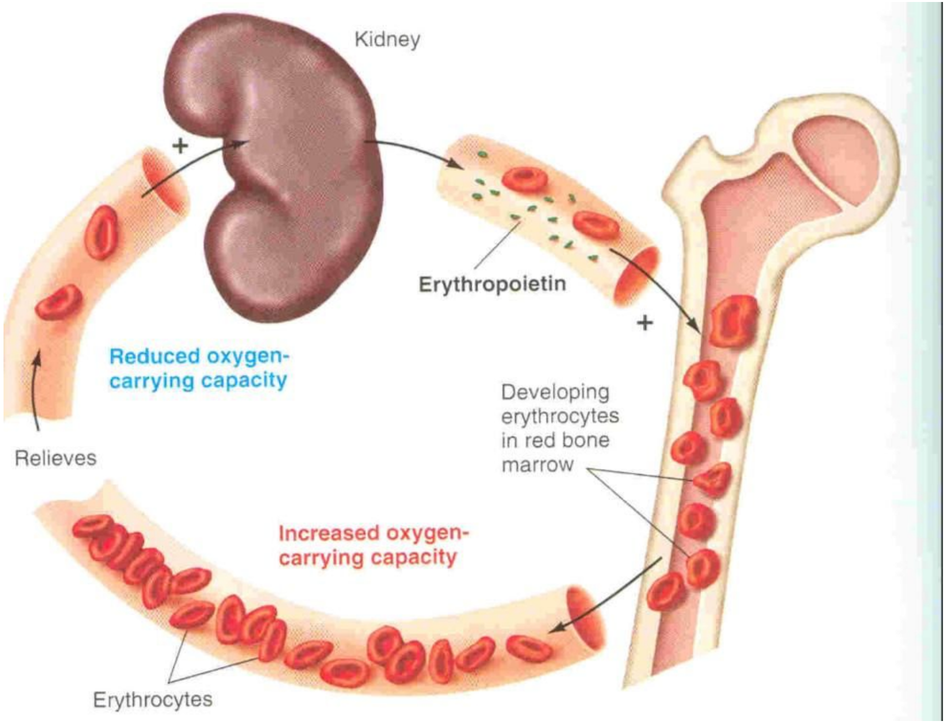
- High altitude
- Heart failure
- Lung Disease

❖ Result in High erythropoietin levels and polycythemia

Clinical Correlation:
In severe renal diseases, the person becomes invariably very anemic as the liver cannot compensate for the role of kidneys in the release of erythropoietin. Anemia of renal disease is treated with erythropoietin



Role of the kidneys in RBC formation



Hemoglobin (Hb)

- Hb molecule consists of 4 chains
- Each formed of heme & polypeptide chain (globin)
- Globular protein

Accounts for >95% of protein in RBC

Main Functions: Transportation of respiratory gases. It carries ~98.5% of all O2

Hb Content of Blood:

Concentration of Hb in the Blood:

Measured as g/dl (grams per deciliter, or 100ml)

Average Values:

- **Male**: 13.5-17.5 g/dl (16 g/dl)
- **Female**: 12-15.5 g/dl (14 g/dl)
- **Infants**: 14-19 g/dl

Concentration of plasma proteins = 7 g/dl

Function of Hb:

In girls' slides: Hb binds CO2 to form carboxyhemaglobin.
In boys' slides: Hb binds CO2 to form carbaminohemoglobin.

1. Gases transport (O2 & CO2)

Hb binds O2 or form oxyhemoglobin
Hb binds CO2 to form carbaminohemoglobin

1. Buffeer (balances the ph)

Structure:

Composed of 4 subunits, each unit contains Heme (iron-porphyrin)
Iron in the heam is ferrous (Fe^{2+}), combines reversibly with oxygen

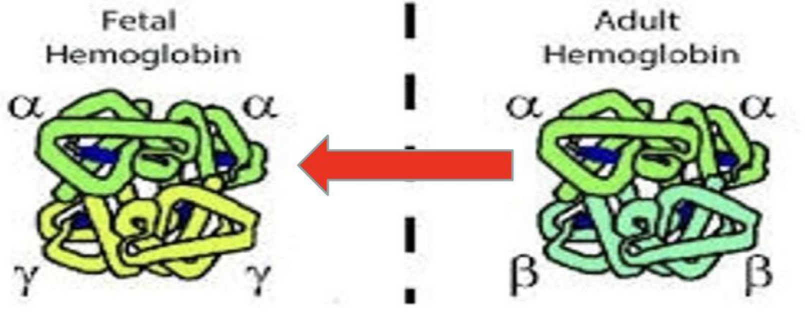
Each gram of pure hemoglobin is capable of combining with 1.34 ml of oxygen

Therefore, in a normal man a maximum of about 20 milliliters of oxygen can be carried in combinational with hemoglobin in each 100 milliners of blood, and in a normal woman 19 milliliters of oxygen can be carried

Types of Hemoglobin

Hb - A (Adult Hemoglobin)	Hb - F (Fetal Hemoglobin)	Hb - A2
-2 alpha + 2 beta chains (98%)	-2 alpha + 2 gamma chains - Has higher affinity for oxygen that Hb-A	-2 alpha + 2 delta chains (2%)

Note442:
Delta chain in Hb-A2 can turn into beta chain in order to make Hb-A



Hb – F
2 alpha + 2 Gamma chains
Has higher afininty for Oxyhen than Hb - A

Hb - A
2 alpha + 2 beta chains

Only Boys Slide

Abnormal types of Hemoglobin

Abnormality in the polypeptide chain results in abnormal Hb [hemoglobinopathies]

Thalassemia

Deceased synthesis in the globin in polypeptide chains
(low hemoglobin)

Sickle cell disease

Abnormal sequence of the amino acids in the globin polypeptide chains

Effects of erythropoietin

Importance:
Tissue oxygenated is the most essential regulator of the RBC's production. The mechanism is via the stimulators effects of hypoxia on the release of erythropoietin hormone

Nature:
Glycoprotein with molecular weight = 34,000

Site of Action:
Bone Marrow

Site of release:
Mainly from the kidney (renal cortex) 90%
Small amount from the liver 10%

Measured In:
In plasma and urine

Site of Action:
Bone Marrow

Action:
Stimulate the growth and differentiation of hematopoietic stem cells (early stem cells)
Doesn't affect maturation process

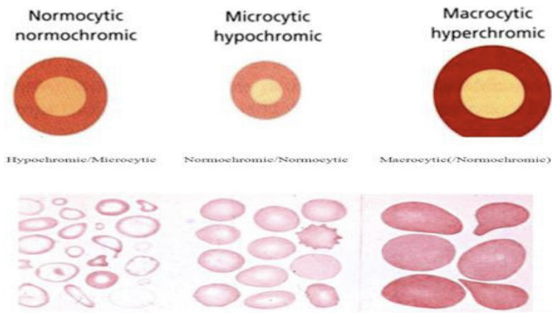
Only Boys Slide

Types of Anemia

	Normocytic (Normochromic)	Microcytic (Hypochromic)	Microcytic (Hypochromic)
Causes	Aplastic Anemia Hemolytic Acute Hemorrhage	Iron Deficiency Anemia	Folate or Vitamin b12 Deficiency
MCH **Mean Cell Hemoglobin**	Normal	Small	Large
MCV **Mean Cell Volume**	Normal	Low	High

Cytic: Size of RBC
-Normo=Normal
-Hypo=Smaller
-Hyper=Larger

Chromic: Color of RBC
-Normo= Normal
-Hypo=Lighter Red (Low Hemoglobin)
-Hyper=Darker red (High Hemoglobin)

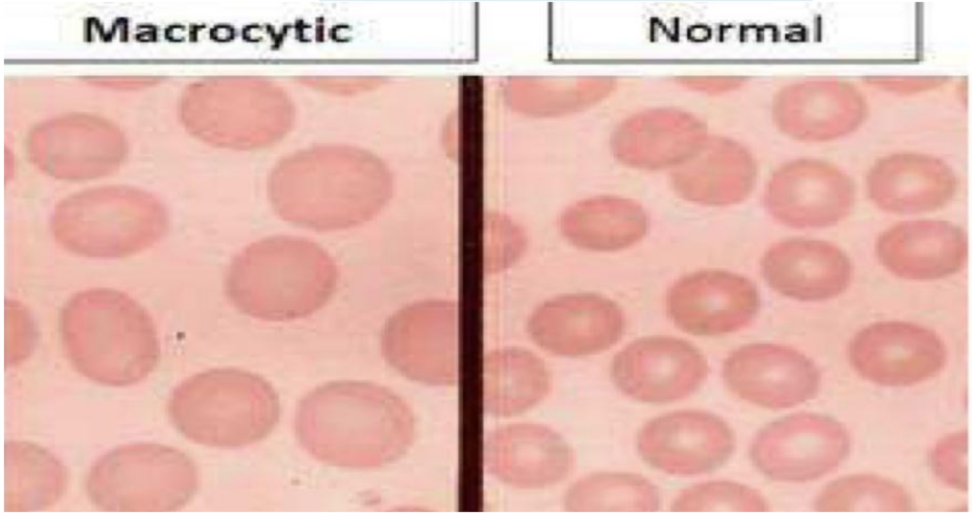


Vitamin B12

Vitamin B12

Origin	Animal Sources only (Meat, Liver)
Importance	Maturation factors for the RBC Essential for DNA synthesis and maturation
Storage	In the liver (In large amounts enough for 3-4 years)
Absorption	Intrinsic Factor is secreted from the stomach to bind to vitamin b12 and helps its absorption (Absorption occurs in the terminal ileum) Some Macrocytic anemia occurs in: 1. Distal small intestinal diseases 2. Autoimmune Deficiency of intrinsic factor (pernicious anemia)

Manifestation of Deficiency	Macrocytic (Megaloblastic anemia) Abnormal large & Fragile Cells
Causes of Deficiency	1-Defective Absorption (Pernicious Anemia) 2-Defective Storage (Liver Disease) 3- Dietary Deficiency (Very Rare)



Folic Acid

Folic Acid

Origin	Animal and Plant Sources (meat, liver, fruits, vegetables). Easily destroyed when cooked
Importance	Maturation factors for the RBC Essential for DNA synthesis and maturation
Storage	In the liver (In very small amounts) 442: it is stored for (1-2 months) and at maximum 3 months
Absorption	Mainly in Jejunum
Causes of Deficiency	1- Dietary Deficiency (Important Cause) 2-Defective Absorption 3-Defective Storage
Manifestation of Deficiency	Macrocytic (Megaloblastic anemia) Abnormal large & Fragile Cells

Role of Different Organs in Erythropoiesis

Role of Liver:
Site of storage or synthesis of different substances

Synthesis of:
1)Globen (Protein part of hemoglobin)
2) 15% of erythropoietin

Storage:
1)Vitamin B12
2)Ferritin (Storage form of iron)

Role of Bone Marrow:
Failure of the bone marrow to produce RBCs is known as (aplastic anemia)

Commonly associated with pancytopenia (decreases production of all types of blood cells)

Treatment depends on the cause

Role of the Kidney: Release of erythropoietin

MCQs

1-Which type of hemoglobin has the highest affinity to oxygen?			
A- Hb-A	B-Hb-F	C-Hb-2A	D- Hb-d
2-first 3 months of embryo nucleated RBCs are formed?			
A- yolk sac.	B- Blood	C- Liver	D- Spleen
3-Where does folic acid get absorbed?			
A- Dudonem	B- Jejunum	C- Ileum	D- None of the above
4-A man found his RBc's are Macrocytic =, he is probably having …….. deficiency?			
A- Iron	B- Vitamin B12	C- Vitamin c	D- None of the above

4-C

3-B

2-A

1-B

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