Lecture: 1

Red Blood Cells (RBCs)

Objectives:

1. Composition of the Blood
2. Functions of the Blood
3. Morphological Features of RBCs.
4. Production of RBCs
5. Regulation of production of RBCs

BLOOD COMPOSITION

1. Cellular components
   - Red Blood Cells (Erythrocytes)
     Erythro : Red Cyte : Cell
   - White Blood Cells (Leucocytes)
     Leuco : white
   - Platelets (Thrombocytes) الصفائح الدموية

2. Plasma
   - •

98% water, ions, plasma proteins (Albumin, globulin, Fibrinogen)
Same ionic composition as interstitial fluid

FUNCTIONS OF BLOOD

1. Transport:
- **O2,CO2,nutrient,hormones,waste product**

2. Homoeostasis:
- **Regulation of body temperature, ECF pH**

3. Protecting against infections:
- **White Blood Cells, Antibodies**

4. Blood clotting prevent blood loss.

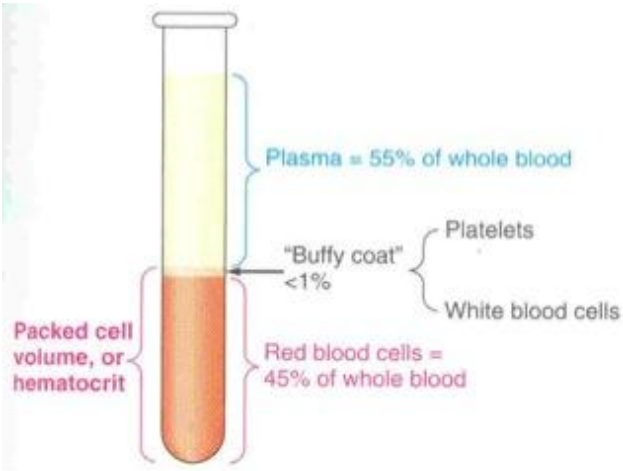
Blood Volume

5 liter in adult

• •

45% is packed cells volume (PCV)
(كمية الدم بالنسبة للبلازما)

55% is plasma volume



Blood Cells Formation

- Erythropoiesis: Formation of RBC (erythrocytes)
- Leucopoiesis: Formation of WBC (leucocytes)
- Thrombopoiesis: Formation of platelets (thrombocytes)

Red Blood Cells

Function of RBC

– O2 transport
– CO2 transport
– Buffer

buffer : chemical substance makes the pH constant

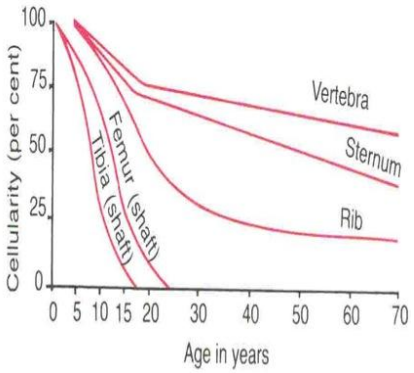
N.B : the buffer in the RBC is Hemoglobin (Hb)

Shape & size

- Flat Biconcave Disc (مسطحة ومقعرة من الجهتين)
-Non-nucleated (خلايا الدم هي الوحيدة التي لا تحتوي على انوية)
-Diameter 7-8 mm x 2.5 mm , 1 mm
-Average volume 90- 95 mm3
-Flexible (مرنه)
-Number =4.7-5 x106 (خلايا الدم الحمراء هي الاكثر وجودةً في الجسم عددها مايقارب ٥ مليون خلية)
-Hb =34g/dl of cells (كمية الهيموجلوبين في كل خلية)
-Hb= 14-16 g/dl in the blood (كمية الهيموجلوبين في الدم)

g/dl - dl : دي سي لتر ، جزء صغير جداً من اللتر مثل ملم

Production of RBC



Sites of RBC Production

- **Early few weeks of embryo nucleated RBCs are formed in yolk sac.**
- **Middle trimester mainly in liver & spleen & lymph nodes.**
- **Last months RBCs are formed in bone marrow of all bones • Bone marrow of flat bone continue to produce RBC into adult life**
- **Shaft of long bone stop forming RBC at puberty while the epiphysis continued to produce RBC**

- في الاسابيع الاولى من تكوين الجنين تتكون خلايا الدم الحمراء وتحتوي على نواة فقط في هذة المرحلة في مكان يسمى **yolk sac**
- في منتصف فترة الحمل تتكون خلايا الدم الحمرهء في الجنين في الاماكن التالية : **liver** الكبد **spleen** الطحال العقد اللمفاوية **lymph nodes**
- في الاشهر الاخيرة من الحمل تتكون خلايا الدم الحمراء في (**bone marrow** نخاع العظم) في جميع العظام.
- بعد الولادة تتكون العظام المسطحة حتى فترة الشباب **adult life**
- يتوقف **shaft** (المنطقة الوسطى من العظام الطويلة) عن تكوين خلايا الدم الحمراء عند سن البلوغ **puberty** ويتحول النخاع بداخله من احمر الى اصفر.
- عند سن البلوغ يتم تكوين خلايا الدم الحمراء فقط في موضعين : **epiphysis** - **flat bones**

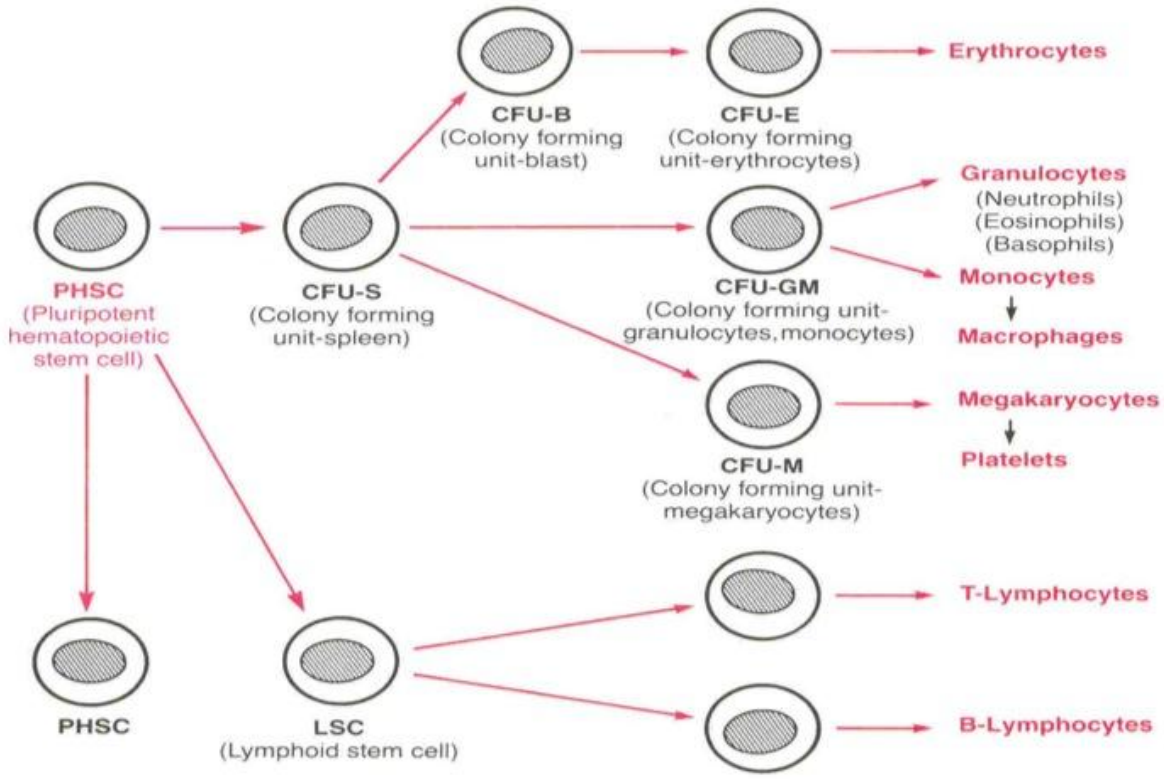
Genesis of RBC

- All blood cell are formed from Pluripotential hematopoietic stem cells committed cells to form RBC, WBC

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

committed stem cells الخلايا الجذعيه
هي المنشأ الرئيسي لخلايا الدم

Genesis of RBC



Stages of differentiation of RBC

• **Committed stem cell**
– Proerthroblast
– basophil erythroblast
– polychromatophil erythroblast
– orthochromatic erythroblast
– **Reticulocytes**
– Mature erythrocytes
• **Rapid RBC production** causes an increase in **reticulocytes in the circulation**

• عملية تكوين خلايا الدم الحمراء تبدأ بـ comitted stem cell وتسمى بخلية دم حمراء ناضجة mature erythrocyte ويقل الحجم تديجياً.
-اهم مرحلة هي reticulocytes

• المعدل الطبيعي ٢٪ اذا زاد فيصبح نخاع العظام اكثر نشاطاً ويفرز كميه اكبر من خلايا الدم الحمراء

Signs of erythrocytes maturation

RBC development is characterize by:

- decrease in cell size
- disappearance of nucleus
- appearance of haemoglobin

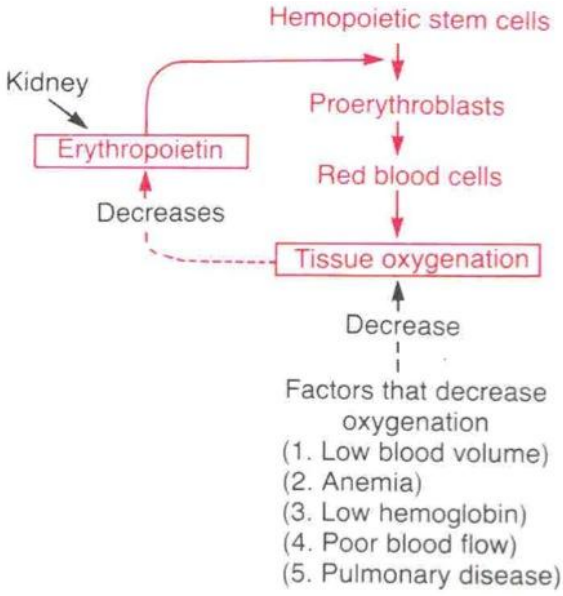
Regulation of RBC production

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

• Hypoxia caused by:
– Low RBC count (Anaemia)
– Hemorrhage
– High altitude
– Prolong heart failure
– Lung disease

• الهرمون المسؤول عن تنظيم انتاج خلايا الدم الحمراء **erythropoietin**
• وهو هرمون يفرز من الكلية **kidney**
• يزيد افرازه في حالات الـ **hypoxia** وهو نقص كمية الاكسجين في الدم

Tissue oxygenation and RBC formation

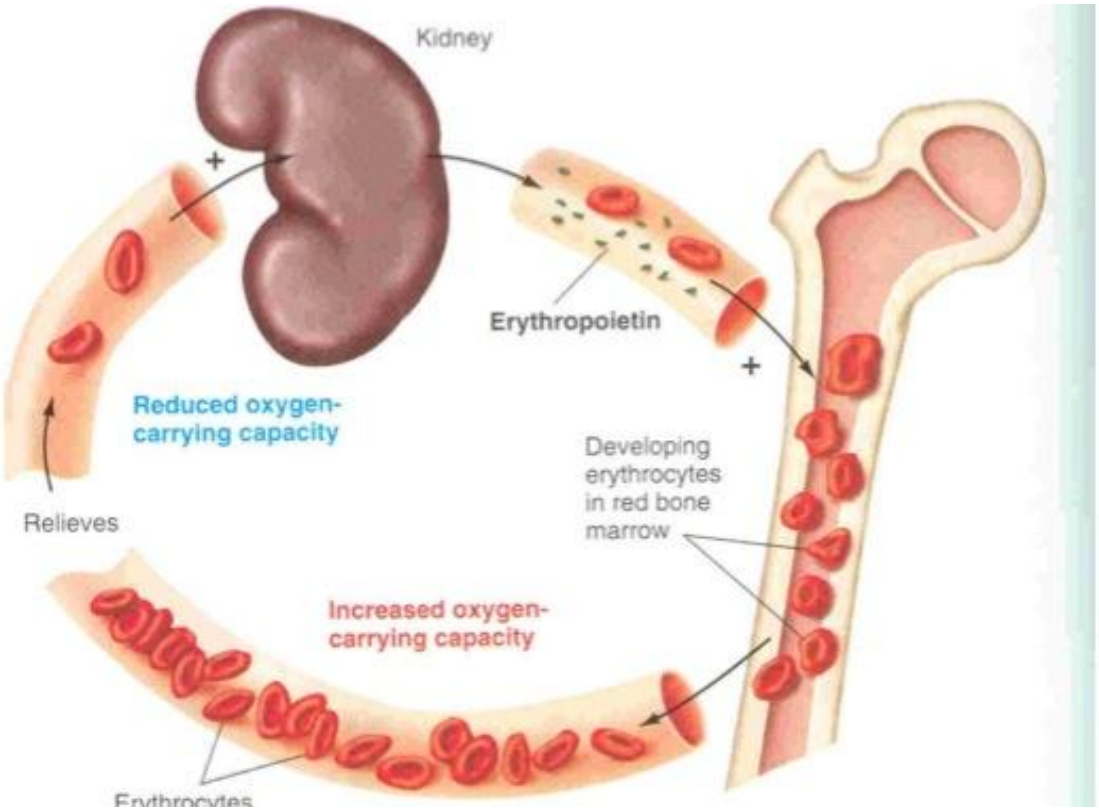


Erythropoietin

- **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**
- **High level of erythropoietin**

– **anemia**
– **High altitude**
– **Heart failure**

Role of the kidneys in RBC formation



Lecture: 2

ERYTHROPOIESIS

Essential elements for RBC's formation & maturation :

- Amino acid : It's the formation of globin in Hb

the deficiency of sever protein leads to Anemia

Result in small RBC's size

- Iron : also formation of Hb

the deficiency of iron leads to Anemia (microcytic anemia)

- Vitamins:

** vit B12 & folic acid (synthesis of nucleoprotein "protein in the nucleus ")

Bigger than the normal cell size

The deficiency of both lead to Anemia (macrocytic anemia)

** vit B6 , Riboflavin ,nicotinic acid , biotin , vit C & vit E.

- Essential elements : copper ,cobalt, zinc, manganese.
- Hormones : androgens , thyroid , cortisol & growth hormones

The deficiency of any one leads to Anemia .

***Vitamin B12 & Folic acid ***

Important for DNA synthesis & final maturation of RBC

Source : meat , milk , liver , fat , green vegetables .

Deficiency of vit B12& folic acid lead to :

- Failure of nuclear maturation & division
- Short life span
- Reduced RBC's count & Hb content
- Abnormally large & oval shape RBC →macrocytic (megaloblastic) anemia

Malabsorption of vit B12

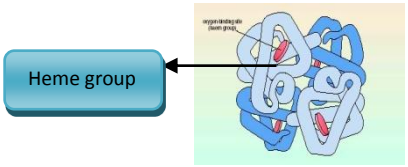
- VB12 absorption needs Intrinsi which secreted by parietal cells of stomach
- VB12 + intrinsic factor is absorbed in the "terminal ileum "

Causes of deficiencies :

1. Inadequate intake .(. غير كافي =inadequate)
2. Poor absorption due to intestinal disease or (stomach disease if it doesn't secrete the intrinsic factor)

Deficiency of B12 due to intrinsic factor & intestinal disease (pernicious anemia)

***HAEMOGLOBIN* (hb)**



Consist of 4 similar subunit each of them formed of :

- Heme (iron): protoporphyrin ring and inside it the (iron)
- Polypeptide chain (globin)

Any change in polypeptide lead to abnormal Hb (hemoglobinopathies) eg , thalassemias & sickle cell .

Functions of HB : hb is the main component of RBC

1) Carriage of O2 " hb bind to O2" →oxyhemoglobin (red color) affect by ph , temp , H+

2) Carriage of CO2 " hb bind to CO2"→ carboxyhemaglobin (blue color)

3) Buffer " chemical substance which prevent the changes in ph"

(Eg . if u add acid it will take the excessive of it , also, iff u add basic it'll take the excessive of it)

Iron metabolism:

Iron is not only for the formation of hb it is also used by anther structures in the body.

The majority of iron is found in haemoglobin around 65%

5%in hems we mean by this heme the one that is found in other structures and enzymes.

Iron absorption:

Iron in food mostly in oxidized form (Ferric) fe^{+3}
There is more oxygen in fe^{+3}
Fe^{+3} can not be observed in stomach &intestine it has to change to fe^{+2} in the stomach by **gastric acid and vit c**
Precence of gastric acid is very important for ions to be obsebed.

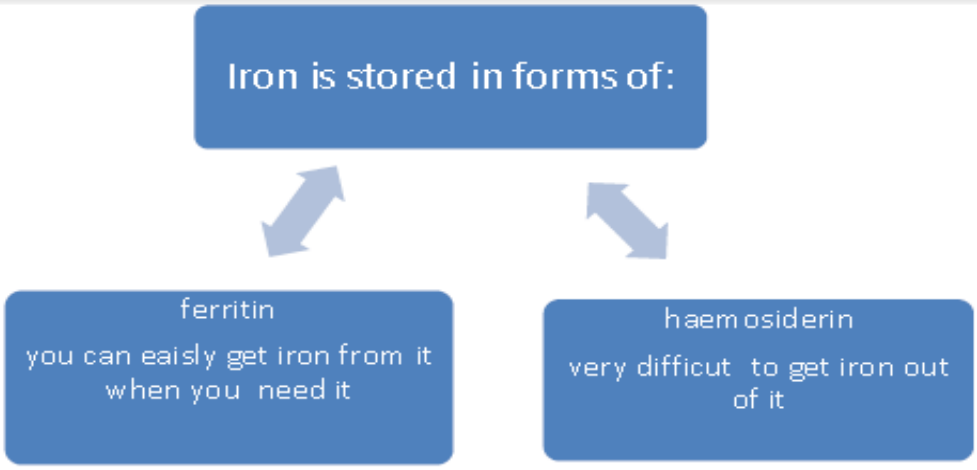
rate of iron absorption:

if there is no iron in your body → absorption ↑

if there is enough iron in your body → absorption ↓

Transport and storage of iron:

Iron is transport in plasma in the form of Transferrin (Apo transferrin +iron) Apo transferrin is also known as beta globulin.



Iron is transported in the blood (plasma) by binding any transporter in the blood

Destruction of RBC:

Rbc have the longest cell cycle.

macrophages :is a type of white blood cells

rbc break down in the spleen by macrophages

the only thing which will be secreted bilirubin

ANAEMIAS:

Symptoms:

Short of breath since hb is low and hb is what carries oxygen

Heart failure when the anaemia is so severe and it left it for a log time

Causes of anaemia:

acute

e.g accident & bleeding

lose big amount of blood over a short time

chronic

eg: ulcer & worms

lose a small amount of blood over a long time

Rbc is formed in the bone marrow

A plastic anemia : a =no \ plastic=cell

Haemolytic anemia : when a lot of rbcs destroy it self before the old age

Spherocytosis : abnormal shape of rbc

-people with sickle cells always have anemia

Polycythemia: opposite for anemia

Primary: the # of rbc increased with out any cause (sort of cancer of rbc)

Secondary:the # of rbc increased due to a certain reason & if we removed that reason rbc will back to normal.

Good luck