MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE
DISTANCE LEARNING CENTER

Lecture № 10

Blood components. Functional role of plasma proteins. Red blood cells, hemoglobin. Hemopoiesis. Blood groups

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* The blood volume is especially important in the control of cardiovascular dynamics.
* The average blood volume of adults is about 7 % of body weight, or about 5 liters.
*About 55 % of the blood is plasma and 45 % is red blood cells, but these percentages can vary considerably in different people, depending on gender, weight, and other factors.

The physical and chemical properties of the blood

❖ red color fluid with suspended blood cells

✓viscosity = 4,0-5,0 (water = 1)

✓pH = 7.35-7.45

✓temperature = 37°C

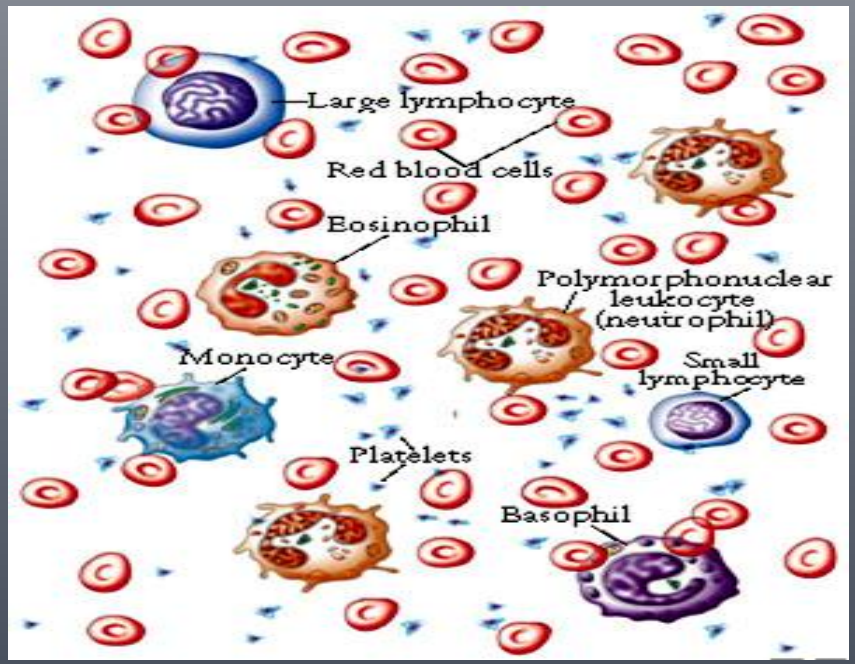
➢blood contains liquid part (plasma) and blood cells

- blood cells:

✓erythrocytes

✓leukocytes

✓thrombocytes



Functions of the blood

- transport of gases, nutrients, and waste products
- regulatory function – transported hormones perform control on functions of all cells of the organism
- homeostatic function – the blood participates in maintenance of constant body temperature, pH, volume and pressure of extracellular fluid
- defensive function – against infections and blood loss

Table 6.3.1 The composition of plasma

Constituent	Proportion/concentration
Water	92% of total volume
Proteins	7% of total volume
Albumin	31–55 g/l
Globulins	23–34 g/l
Fibrinogen	2–4 g/l
Other solutes	
Bicarbonate	21–27 mmol/l
Calcium	2.1–2.5 mmol/l
Chloride	95–103 mmol/l
Magnesium	0.7–1.3 mmol/l
Phosphate	0.9–1.3 mmol/l
Potassium	4.0–5.0 mmol/l
Sodium	135–142 mmol/l
Sulphate	83–125 µmol/l
Ions (total)	260–280 mmol/l
Cholesterol	3.5–6.5 mmol/l
Glucose	4.5–5.5 mmol/l
Iron	13–32 µmol/l
Urea	2.5–6.7 mmol/l
Uric acid	0.18–0.42 mmol/l

60- 80 g/l → COP 28 mmHg (25-30)

Posm ~ 290 mOsm/kg (285-295)

Plasma proteins

❖Plasma proteins are divided into 3 groups:

✓Albumins- 58-60%

✓fibrinogen- 2-4%

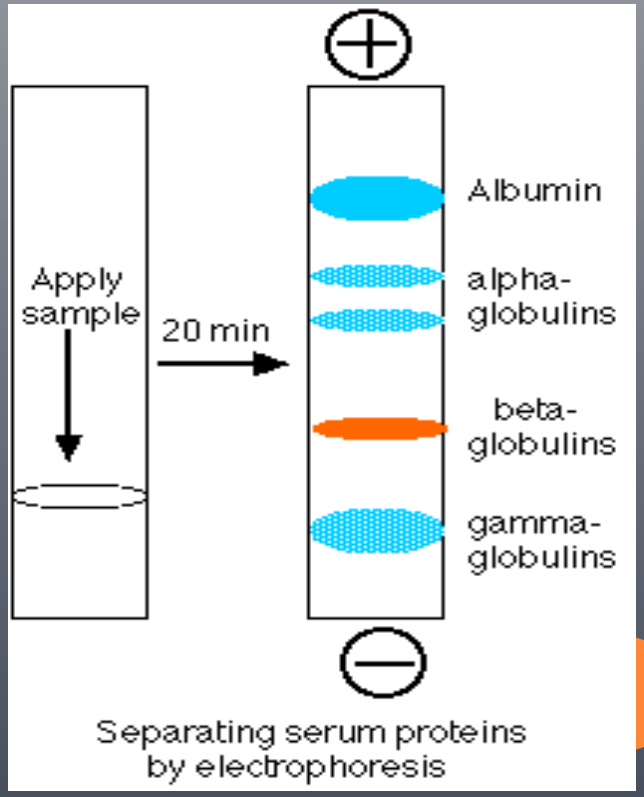
✓globulins - 35-38%

α (α_1,α_2) ß ($ß_1$,$ß_2$) γ

➢the different groups differ each other to molecular weight and the number of electrical charge. This allows their separation on fractions under pH 8.6, using electrophoresis.

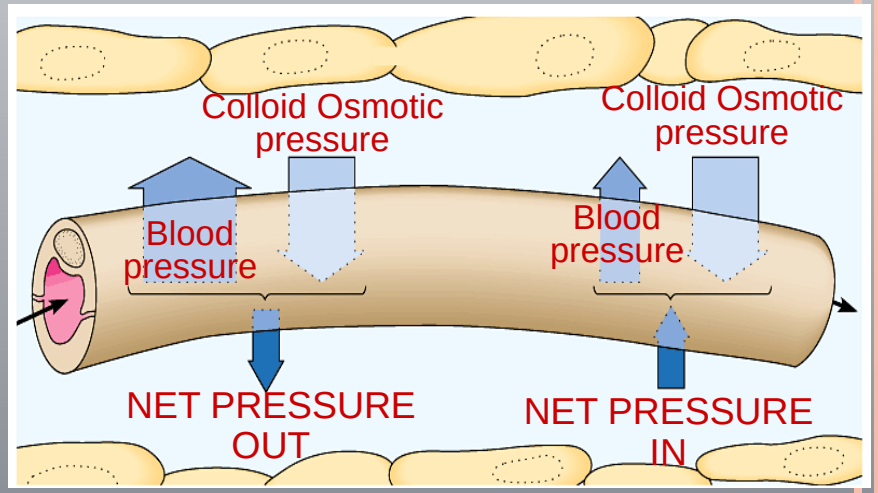
- albumins have the lowest molecular weight and are strongly charged
- γ globulins have the highest molecular weight and are weakly charged. The most of them are antibodies.

❑ all albumins, fibrinogen and 50-80% of globulins are formed into the liver. The other globulins are formed in the lymphatic system.



Separating serum proteins by electrophoresis

Functions of plasma proteins



➢**Albumins** = 32-52 g/l:

✓They determine at high degree (80%) colloid-osmotic (oncotic) pressure of the plasma, on which transport of water across capillary walls depends.

✓transport of hormones , bilirubin,FFA, drugs
✓storage of AA that may use during starvation
✓they are buffer system of the blood

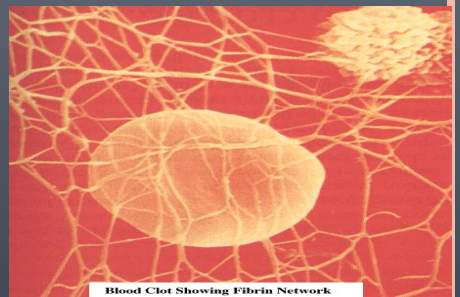
➢**Globulins** - 23-35 g/l heterogenic group with different functions:

✓α, ß – for transport of Fe, Cu, hormones, vitamins (A, D, E, K), lipids

✓γ – antibodies against foreign antigens,

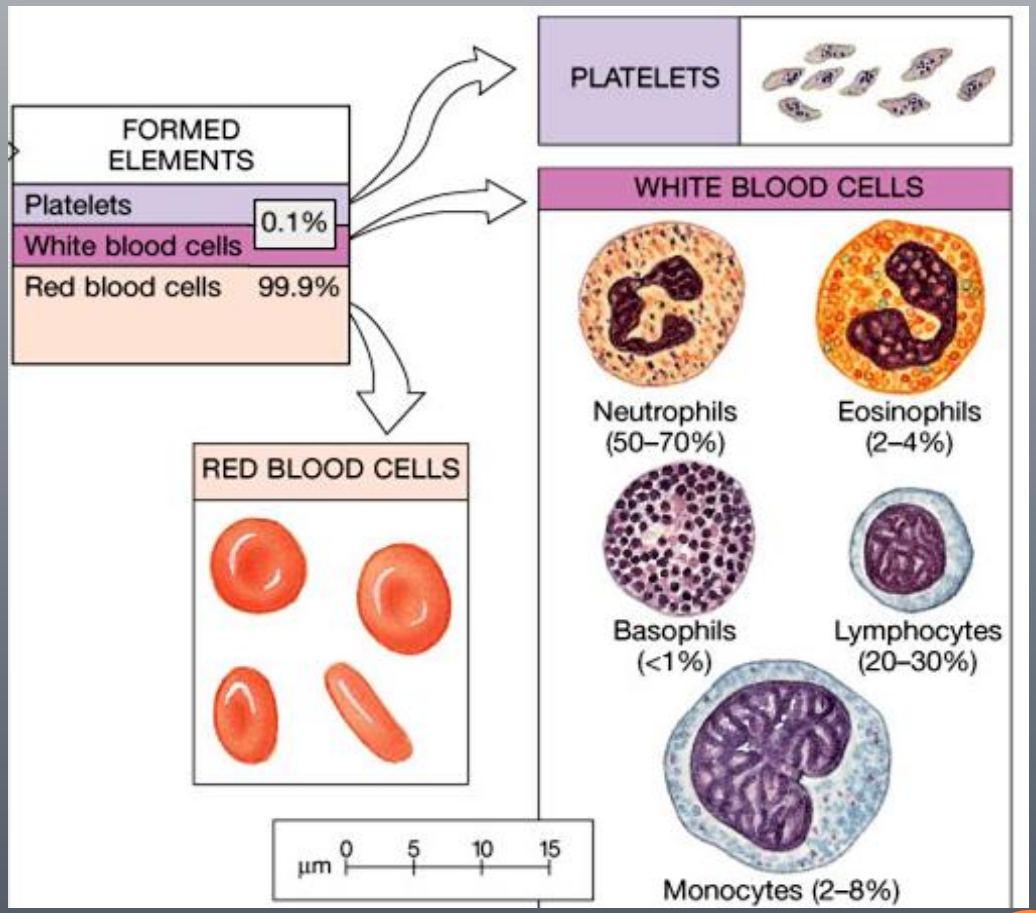
they perform humoral immunity

➢**Fibrinogen** – participates in hemocoagulation



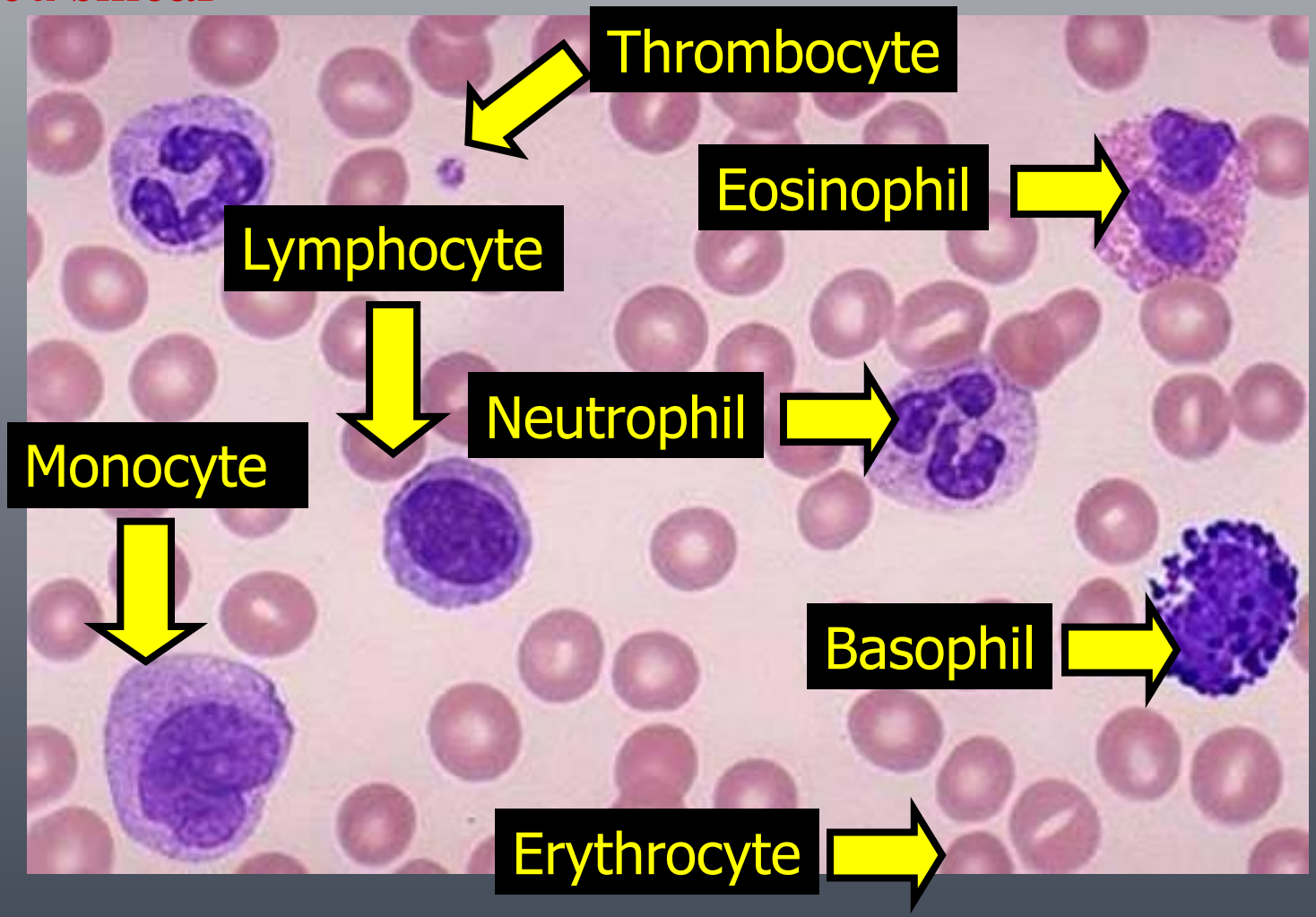
Blood cells

- erythrocytes
- leukocytes
- thrombocytes (platelets)



Tests for blood cells determination

- determination of number of blood cells – electronic or chamber blood cells counting
- determination of the type of blood cells – preparation and watch of blood smear



❖ Hemopoiesis is the process of Production of Blood Cells.

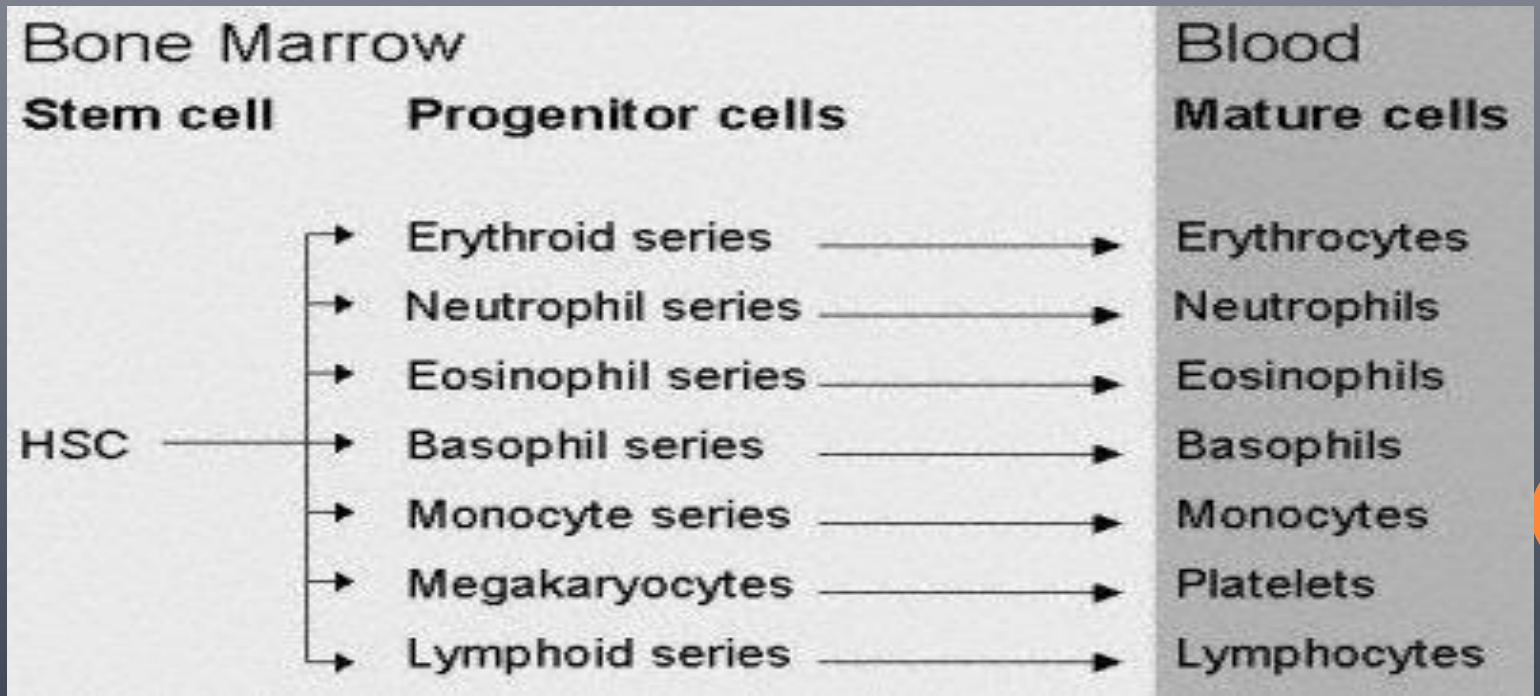
➢There are 2 types of hemopoiesis:

✓*constitutional*:

▪ Constant creation of blood cells with the rate maintaining their normal number in the blood ~ 10^{13} blood cells per day.

✓*induceble*:

▪ Acceleration of hemopoiesis because pathological decrease of number of blood cells. It is specific – only increased production of type of blood cells that is lower than normal occurs.

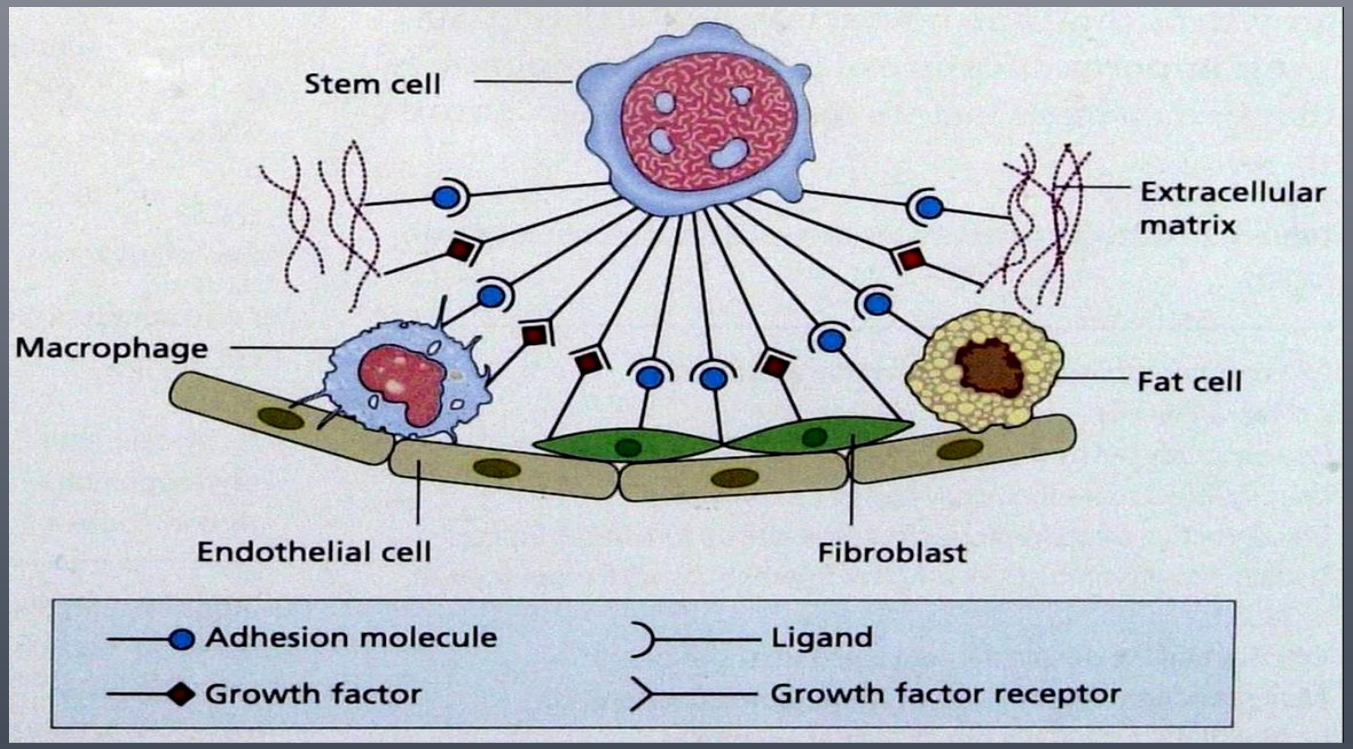


Hemopoiesis in bone marrow

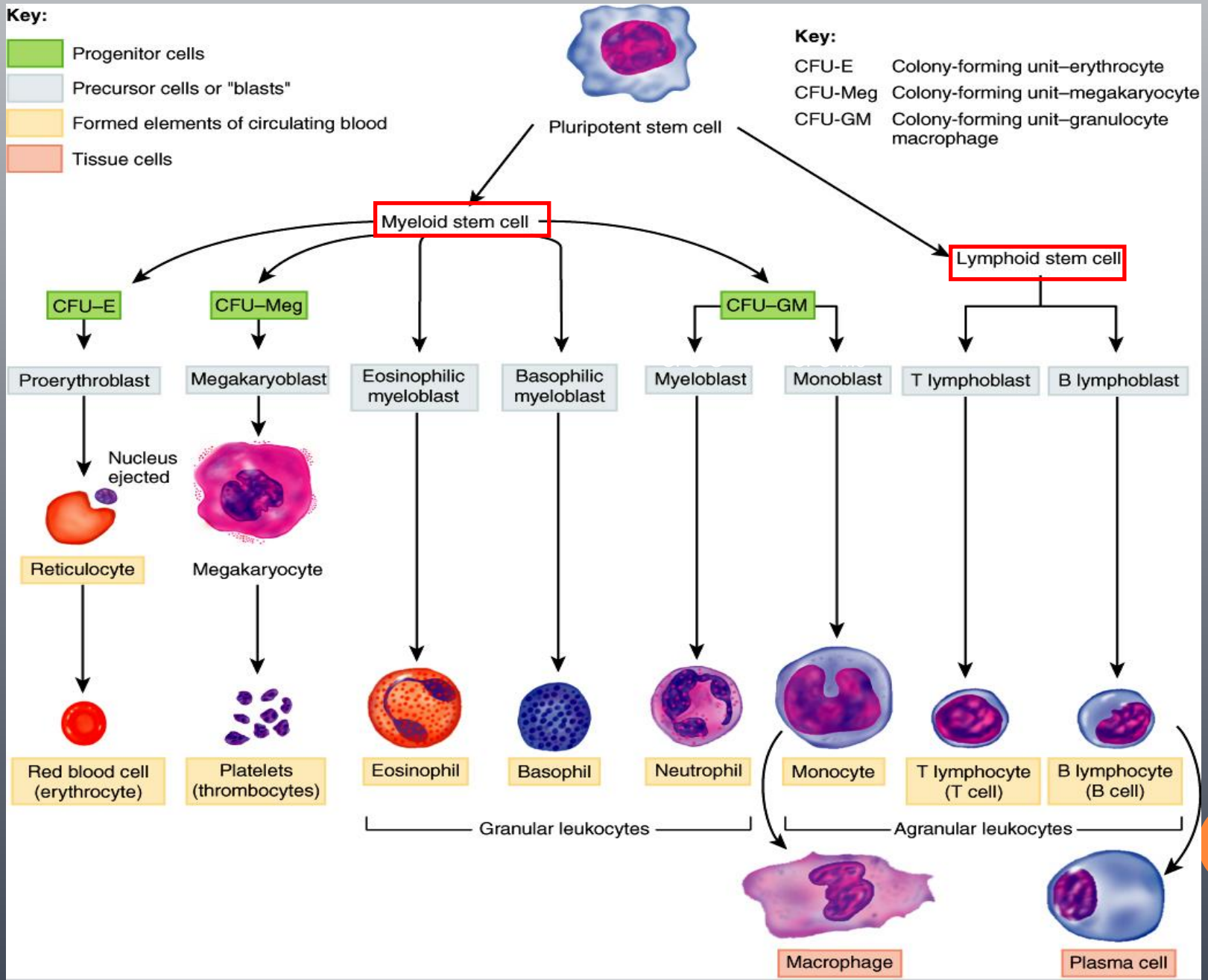
➢Stroma of bone marrow contains the cells (fibroblasts, macrophages, fat cells) and extracellular matrix (fibronectin, laminin, colagene) to which are bound adhesion molecules and growth factors.

- Stem cells have specialized receptors for them.

❑ Interaction between stem cells and stroma is important for normal hemopoiesis.

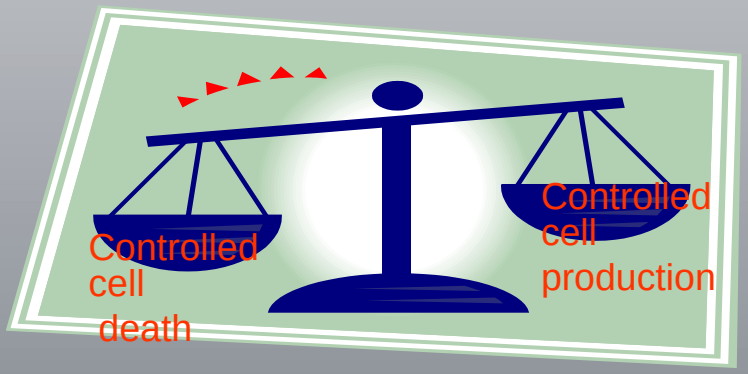


Hemopoiesis



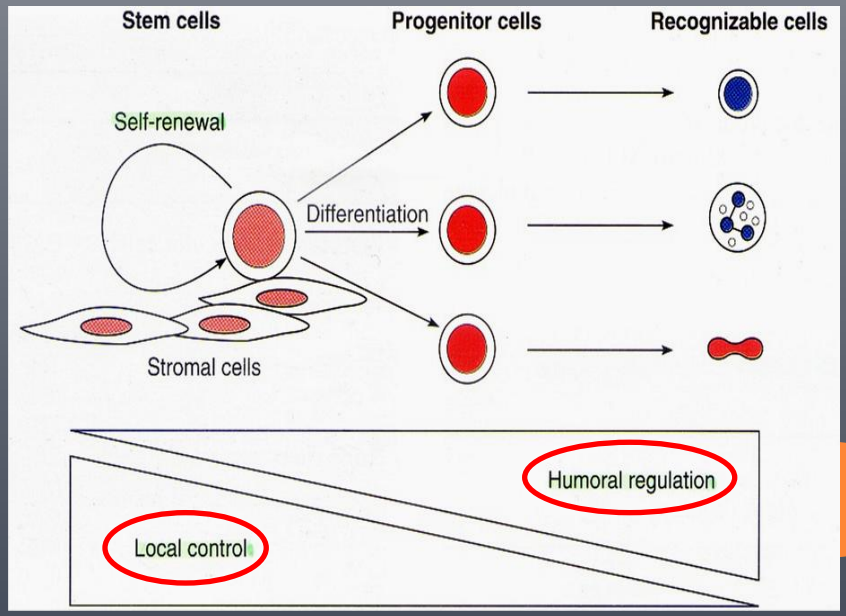
Control of hemopoiesis

❖ Control of hemopoiesis ensures exact balance between the rate of cell production and the rate of controlled cell death.



❖Control uses local and humoral mechanisms.

➢The local mechanisms include interaction between hemopoietic cells and stroma of bone marrow, and are important in early phases of hemopoesis.



- Humoral mechanisms of control are performed by hemopoetic growth factors that are secreted by the cells of bone marrow, kidney and liver.
- Hemopoietic growth factors are glycoproteins from family of citokines.
- Colonia-stimulating factors: SCF (stem cell factor) LIF (leucocyte inhibitory factor) GM-CSF (granulocyte /macrophage), MEG-CSF
- trombopoietine
- erythropoietine
- interleukins (IL-1, IL-3, IL-4, IL-5, IL-6, IL-7, IL-11)

Red Blood Cells (Erythrocytes)

❖Functions of RBC:

¤ The major function of red blood cells, also known as *erythrocytes, is to transport hemoglobin, which in turn carries oxygen from the lungs to the tissues.*

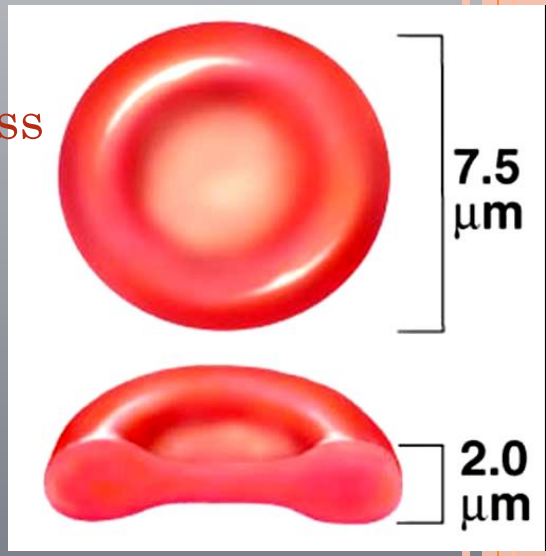
¤ They contain a large quantity of *carbonic anhydrase, an enzyme* that catalyzes the reversible reaction between carbon dioxide (CO_2) and water to form carbonic acid ($H_2 CO_3$), increasing the rate of this reaction several thousand fold. The rapidity of this reaction makes it possible for the water of the blood to transport enormous quantities of CO_2 in the form of bicarbonate ion (HCO_3^-) from the tissues to the lungs, where it is reconverted to CO_2 and expelled into the atmosphere as a body waste product.

¤ The hemoglobin in the cells is an excellent *acid-base buffer (as is true of most proteins), so that the red* blood cells are responsible for most of the acid-base buffering power of whole blood.

Shape and Size of Red Blood Cells

➢number of RBC - 4.5 - 5.9.10^{12}/l ♂ and 4.2 - 5.2.10^{12}/l ♀

Shape - Normal red blood cells are biconcave discs having a mean diameter of about 7.8 µm and a thickness of 2.5 µm at the thickest point and 1 µm or less in the center. This shape ensures well diffusion of gases. The shapes of red blood cells can change remarkably as the cells squeeze through capillaries.



➢90-95% of dry substance is due to Hb;

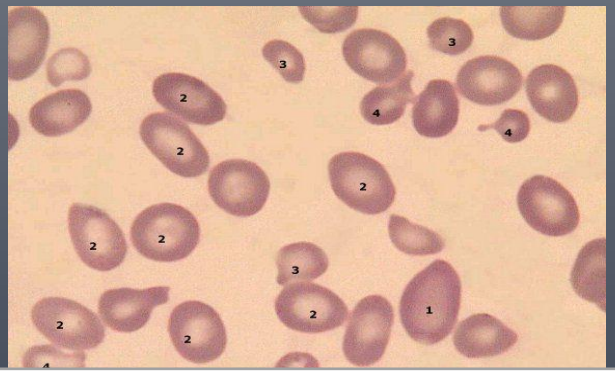
➢MCH=29±2,5pg

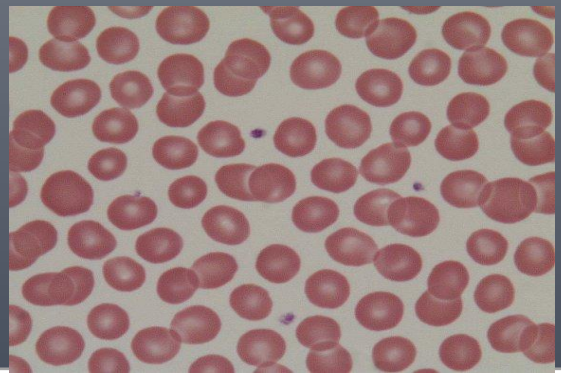
➢MCHC = 320 – 360 g/l erythrocytes

➢MCV~90 (82-98) fl

✓MCV> 100 fl - macrocytes

✓MCV< 80 fl - microcytes



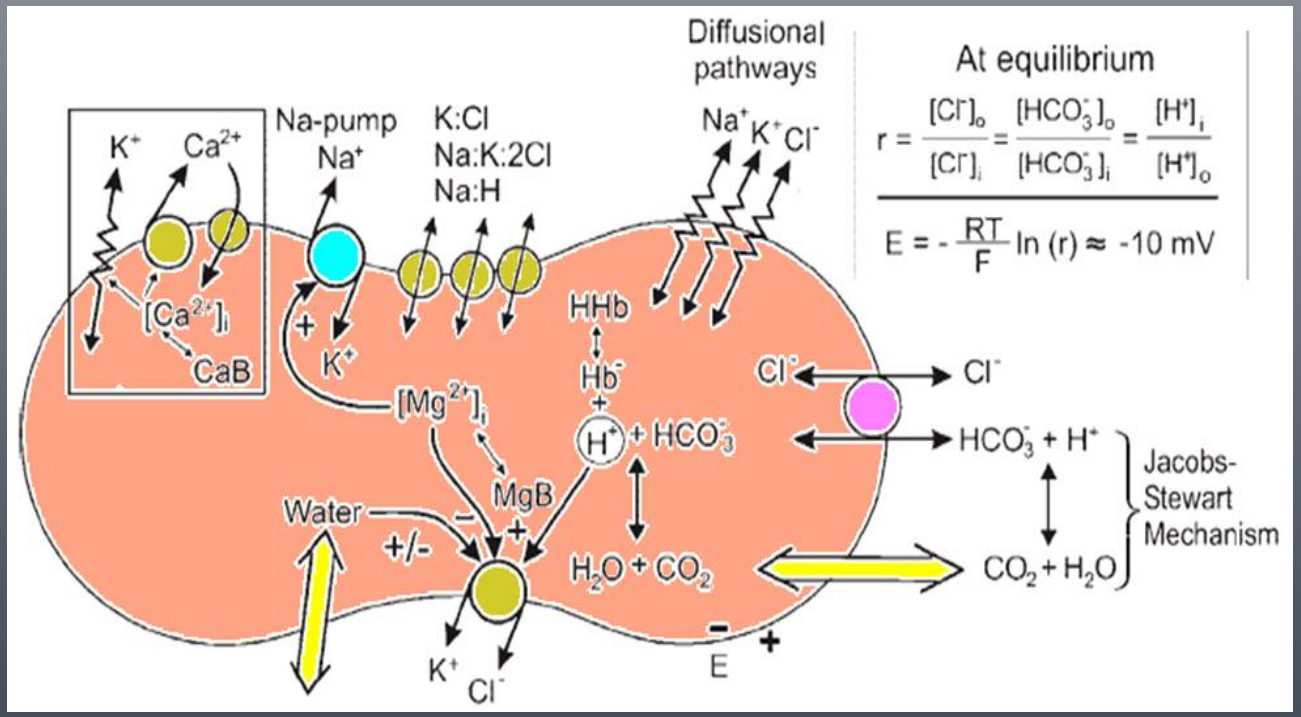


Characteristics of RBC morphology and metabolism:

- they have not nuclei and ribosomes, have not synthesis of proteins
- their life lasts av. 120 days
- they have not mitochondria; the sours of energy is anaerobic glycolysis

- glycolysis has important role for :

✓formation of 2,3-diphosphoglycerate (2,3-DPG) that decreases affinity of Hb to O_2 and increases its removal to the tissues

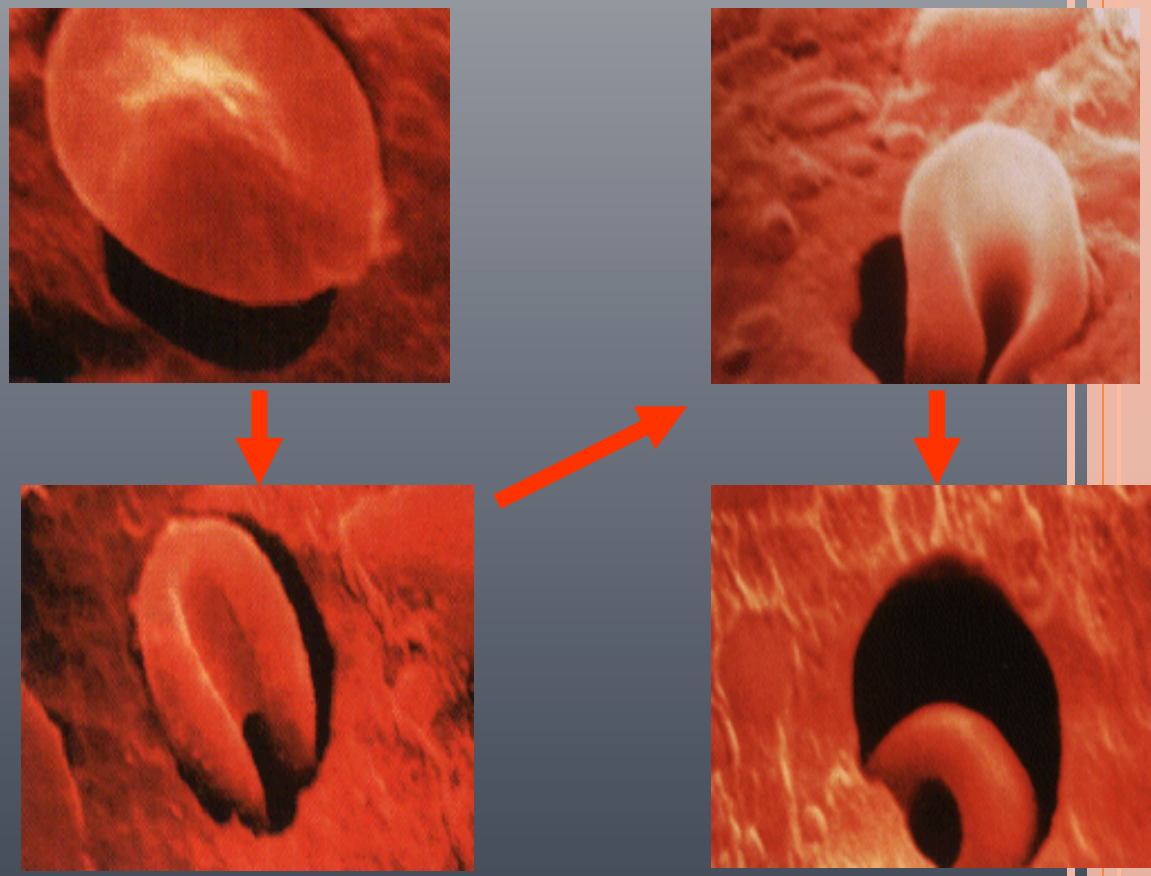


Characteristics of RBC morphology and metabolism:

- Formation of reductors as - NADPH, NADH, reduced glutathione, that are important for reduction of Hb
- They maintain osmotic pressure with low usage of energy (Na-K ATPase), because low permeability of their membrane for Na^+ and K^+ ions
- RBC membrane has high permeability for water and anions (Cl^- and HCO_3^-)
- They exchange rapidly CO_2 and serve as its transporter from the tissues to the lungs

Deformation of RBC membrane

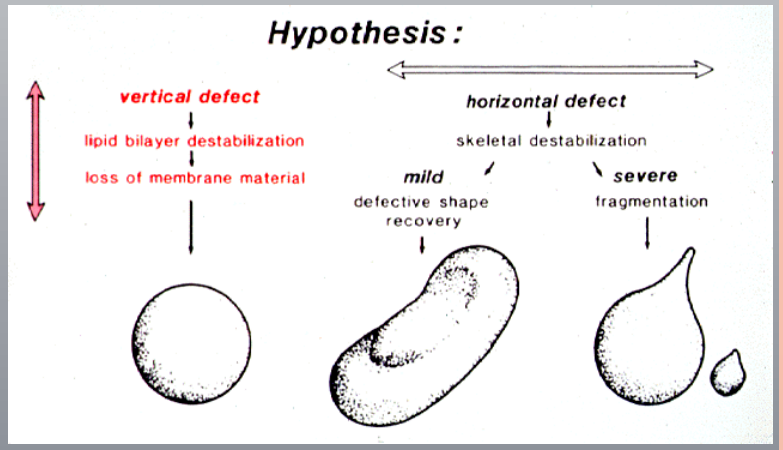
- They can change the shape passing through thin capillaries
- the possibility of deformation depends on:
  - ✓cellular geometry- shape and ratio surface: volume
  - ✓the structure of membrane and cytoskeleton and interaction between them
  - ✓ the content of ATP

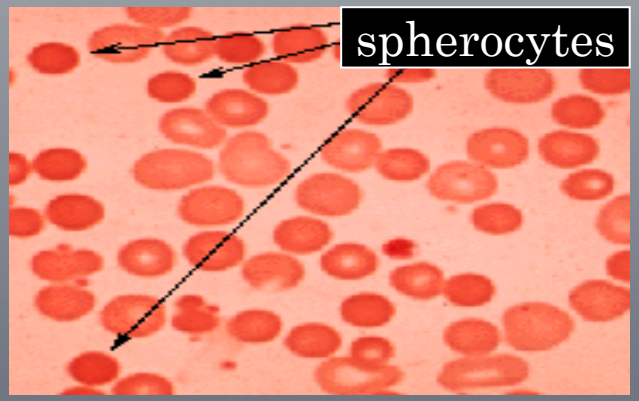


Hemolytic diseases, connected with the abnormal RBC shape

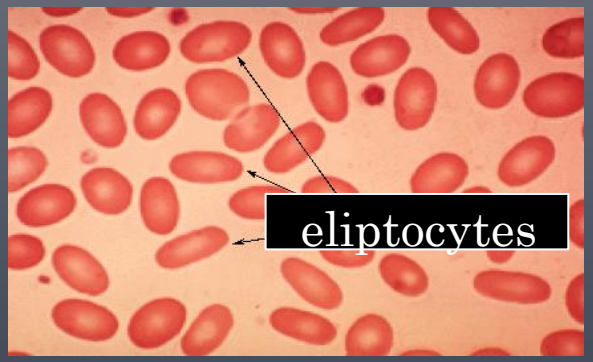
❖ the causes for these diseases are:

➢altered interaction between membrane and cytosckeleton, loss of lipids from membrane and decreased ratio surface:volume

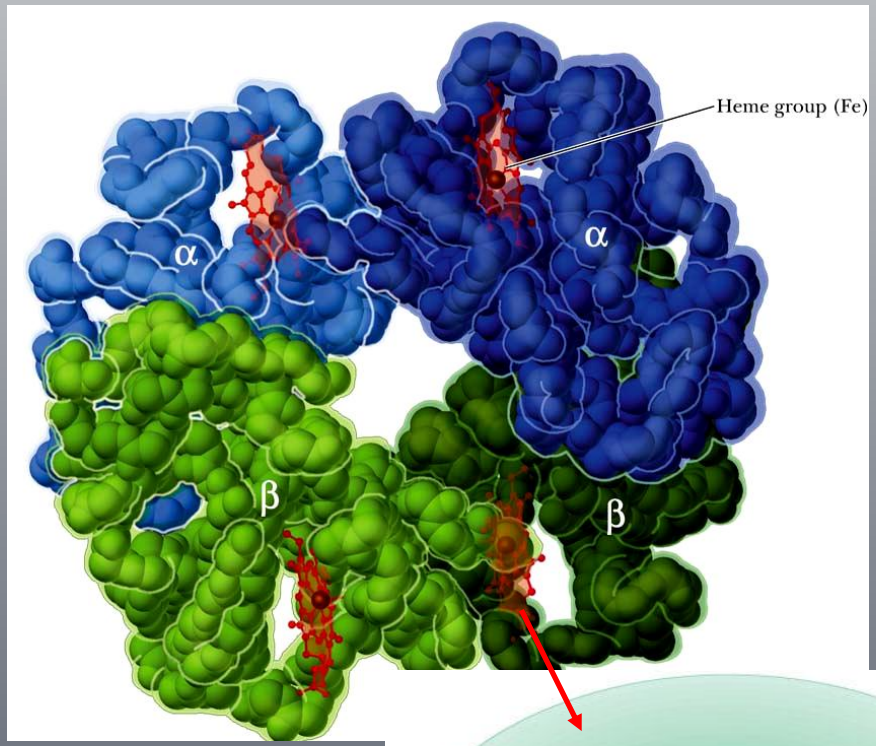


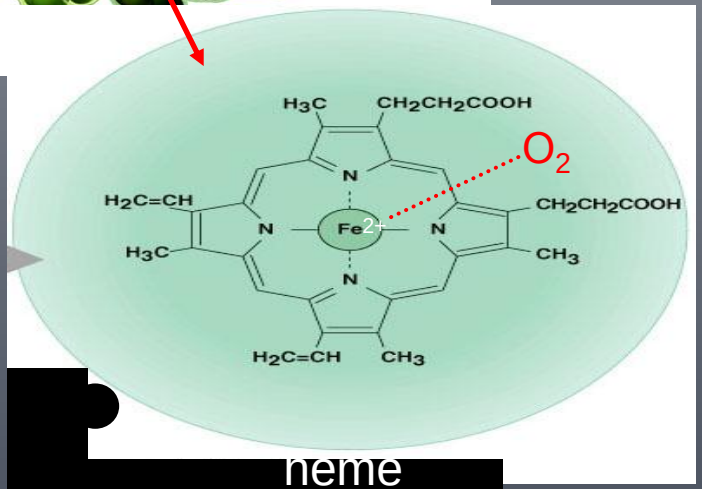


➢disturbance during formation of cytoskeleton (eliptocytosis)



Hemoglobin


Heme group (Fe)
α
α
β
β


H3C
CH2CH2COOH
O2
N
H2C=CH
CH2CH2COOH
N
Fe2+
N
H3C
CH3
N
H2C=CH
CH3
heme

Hemoglobin

❖ functions:

➢transport of O_2 from the lungs to the tissues

➢transport of CO_2 from the tissues to the lungs

➢the most powerful buffer system of the blood

• normal concentration: 160±20 g/l (m) ; 140±20 g/l (f)

❑ Hemoglobin is globular chromoprotein (mw ~64000),

❑Hemoglobin molecule contains 4 subunits

• each subunit contains:

✓Heme – tetrapyrolic ring bound with Fe^{2+}

♦ Fe^{2+} reversely bound O_2 -> oxyhemoglobin

1 heme - 1 mol O_2; 4 hemes - 4 mol O_2

✓globin- polypeptide chain that bound heme and CO_2

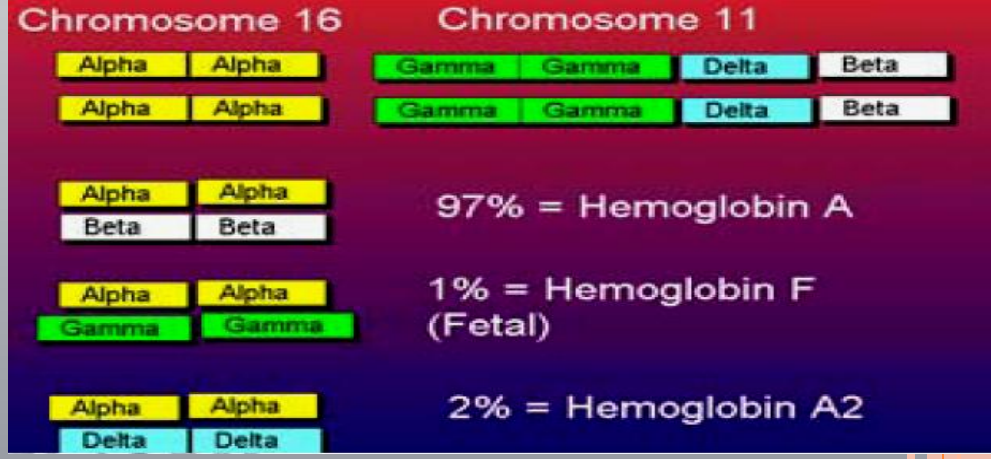
molecule of Hb has 2 sparing polypeptide chains:

◊ Hb A has 2 α and 2 ß chains

Hemoglobin

α chain– chromosome 16;

β, δ, γ chains – chromosome 11



adults

normal

Hb A (95 - 97 %) – α_2, β_2

Hb A_2 (1 – 3 %) – α_2, δ_2

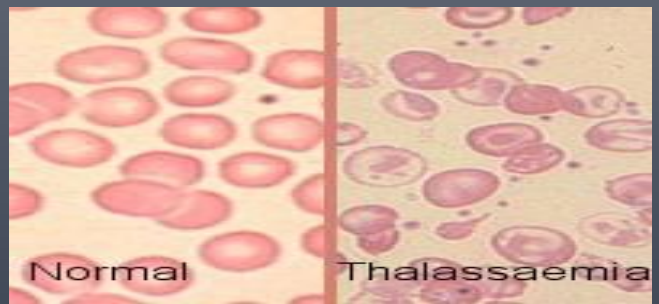
HB F (~ 1 %) – α_2, γ_2

abnormal

Hb S – α_2, β_2^S – glutamat is replaced by valine

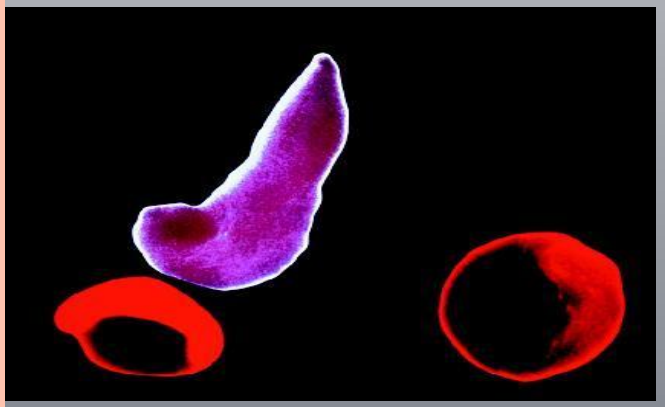
Hemoglobin C – α_2, β_2^C - glutamat is replaced by lisine

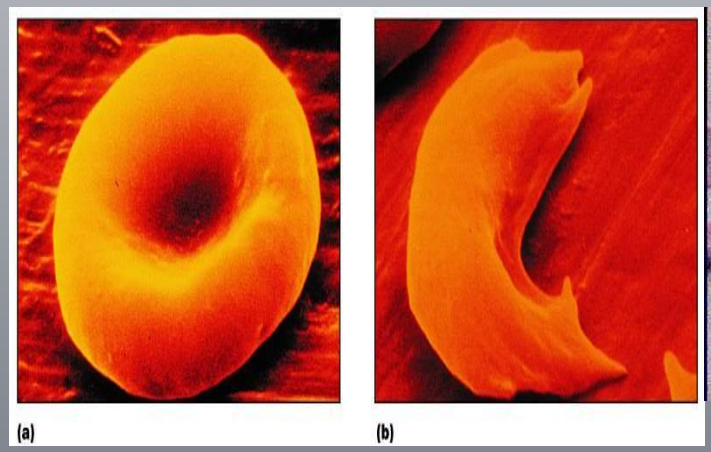
Hemoglobin H (β_4): α-thalassemia

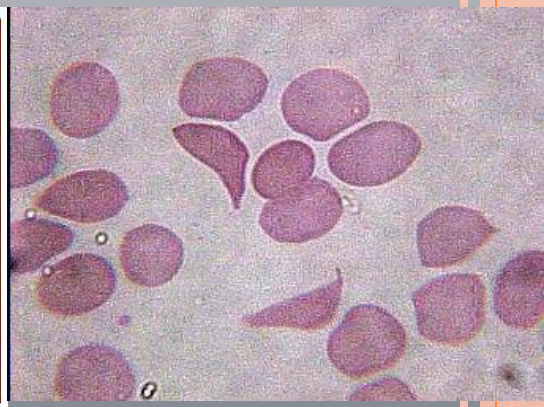


Sickle cell anemia

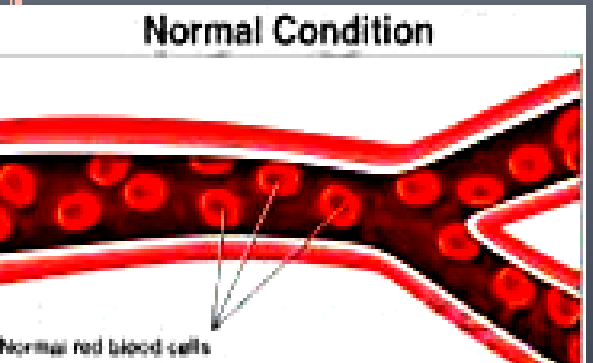
- under low pO_2 β chains of hemoglobin S bound each other and make the big polymers that change the chap of erythrocytes

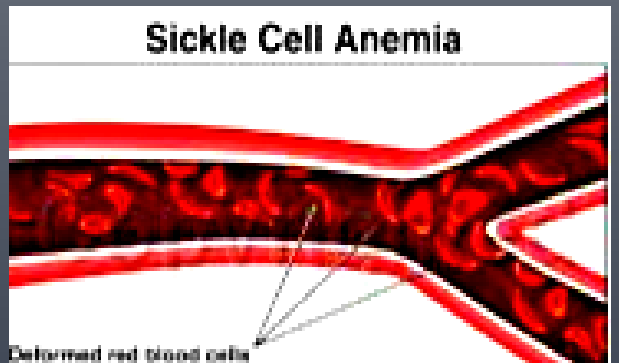


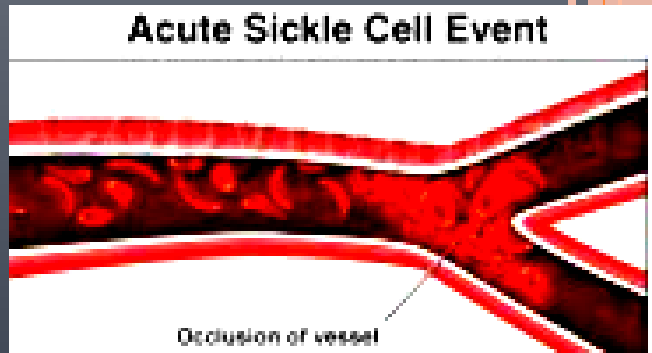




- deformed erythrocytes make aggregats that close the vessels and cause the hemolysis
- hemolytic anemia occurs with hypoxia,because of disturbansed microcirculation



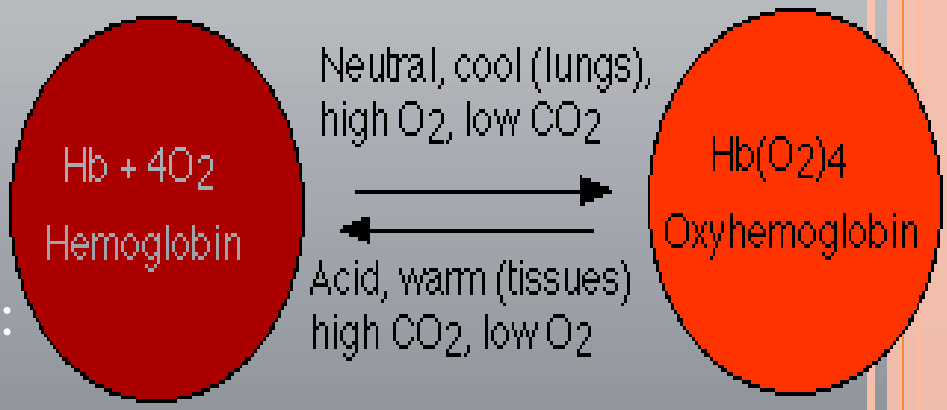




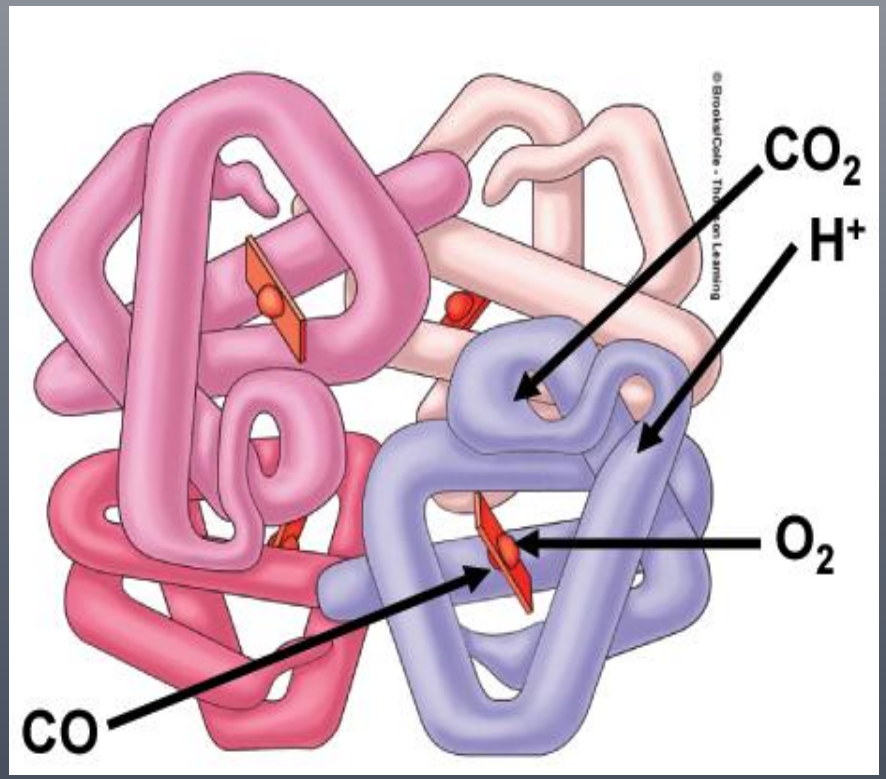
The compounds of hemoglobin

➢ Oxyhemoglobin – combination of Hb with O_2, the iron is Fe^{2+}

✓oxyhemoglobin removes O_2 to the tissues, because of their lower pO_2.



- the removal of O_2 is facilitated by: ↑pCO_2, ↑ 2,3-DPG, ↑ H^+, ↑ T^o



The compounds of hemoglobin

- Carbaminohemoglobin (carbhemoglobin) – combination of Hb with CO_2. CO_2 is bound to globin - transport form of CO_2 from the tissues to the lungs
- Methemoglobin – oxidased form of Hb, Fe^{2+} becomes Fe^{3+} and can not remove O_2.
- Carboxihemoglobin – combination of Hb with CO. CO can bound to the heme with 200 fold higher affinity than this to O_2.

Haematocrit

❖ Hct is the ratio between the volume of erythrocytes to the volume of whole blood.

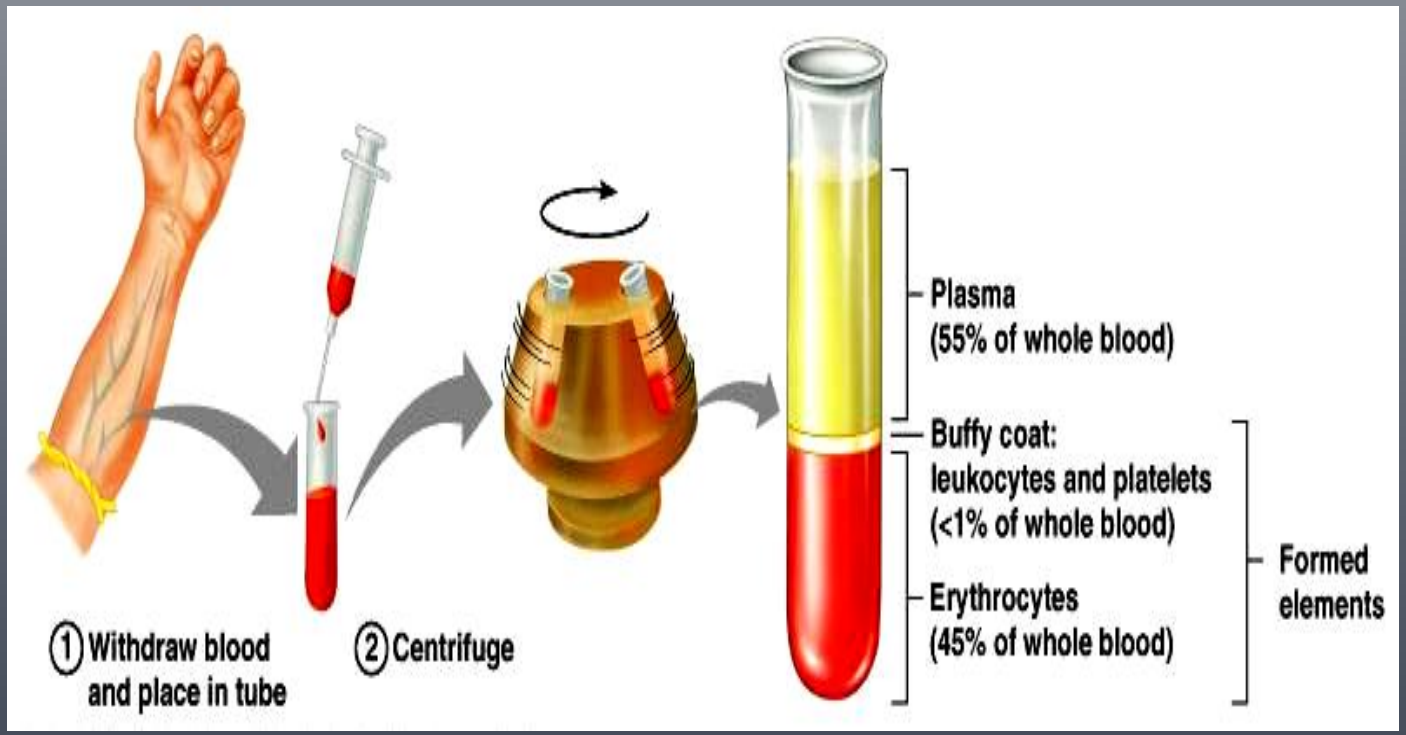
➢normal value: male = 0,40-0,55 l/l ; female = 0,35-0,50 l/l

❑ Hct is changed when:

✓the number of erythrocytes is changed

✓the volume of erythrocytes is changed

✓the volume of plasma is changed



Production of Red Blood Cells

Erythropoiesis occurs in red bone marrow of the membranous bones, such as the vertebrae, sternum, ribs, and ilia.

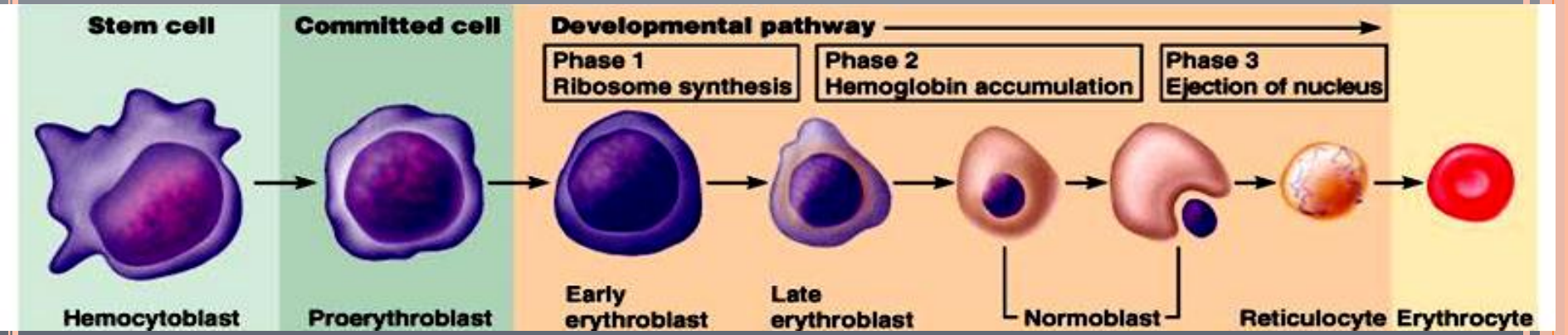
➢erythrocytes are formed from *pluripotential hematopoietic stem cell*:

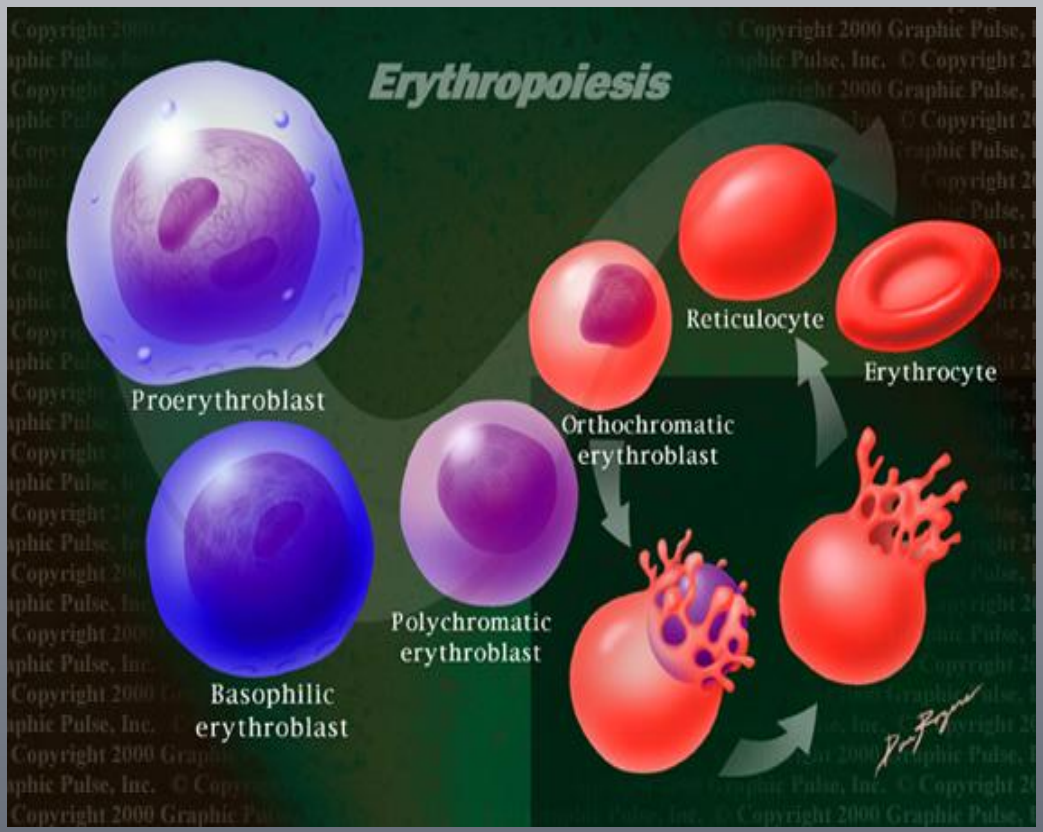
✓BFU-E (burst forming unit-erythroid) or proerythroblast

✓CFU-E (colony forming unit-erythroid) or early erythroblast

✓late erythroblast ✓normoblast ✓reticulocyte ✓erythrocyte

Hematopoietic growth and differentiation inducers influence the different phases.

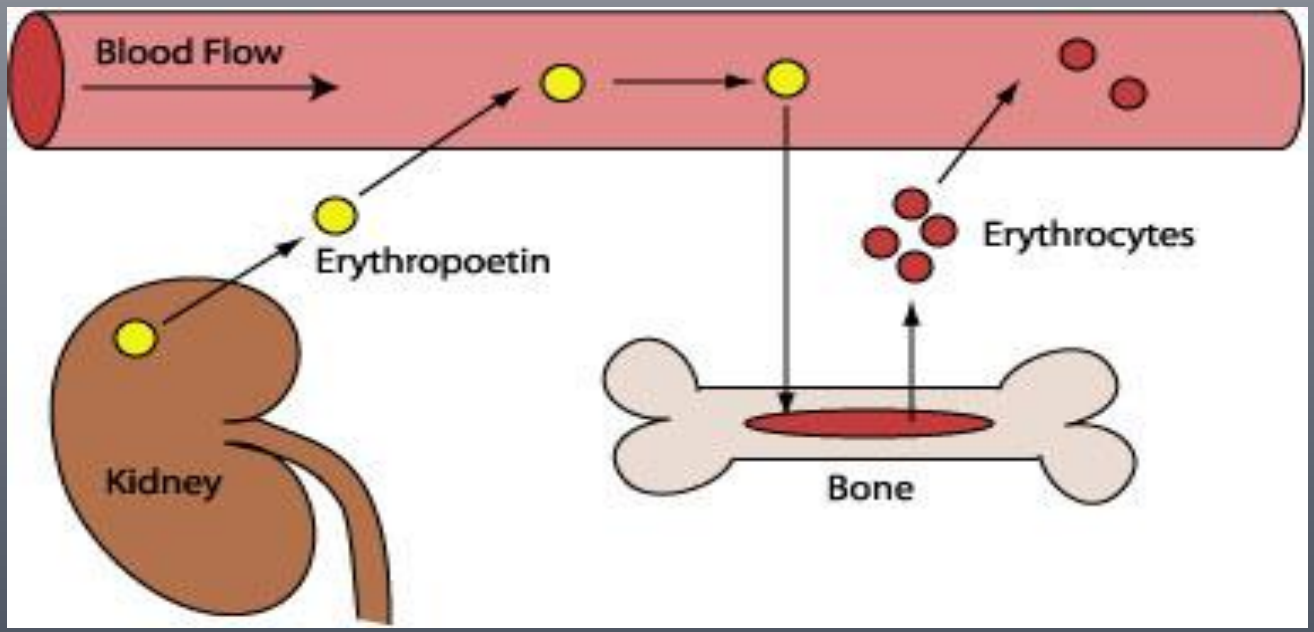




- reticulocytes are av. 0.5 – 2.5 % of erythrocytes in peripheral blood
  - they have ribosomes, rough ER and can synthesize hemoglobin
- for 2 days life in the blood they become erythrocytes
  - their number increase during accelerated erythropoesis

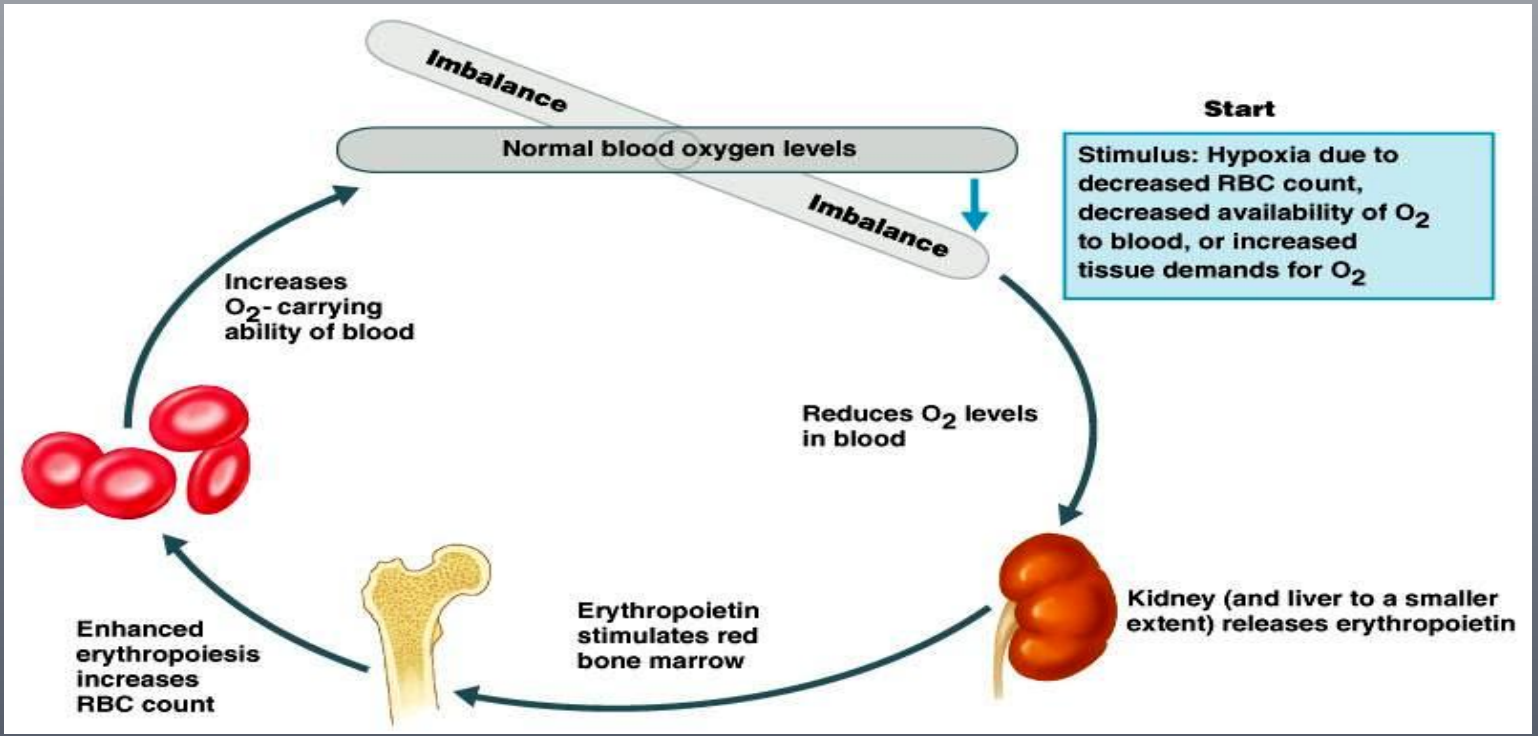
Control of erythropoiesis

- the main regulator of erythropoiesis is erythropoietin
  - it is glycoprotein (mw ~30 κDa)
  - it is synthesized mainly by the peritubular intersthicial cells in the renal cortex and outside medulla and small quantity (10-15%) by the liver



Control of secretion of erythropoietin

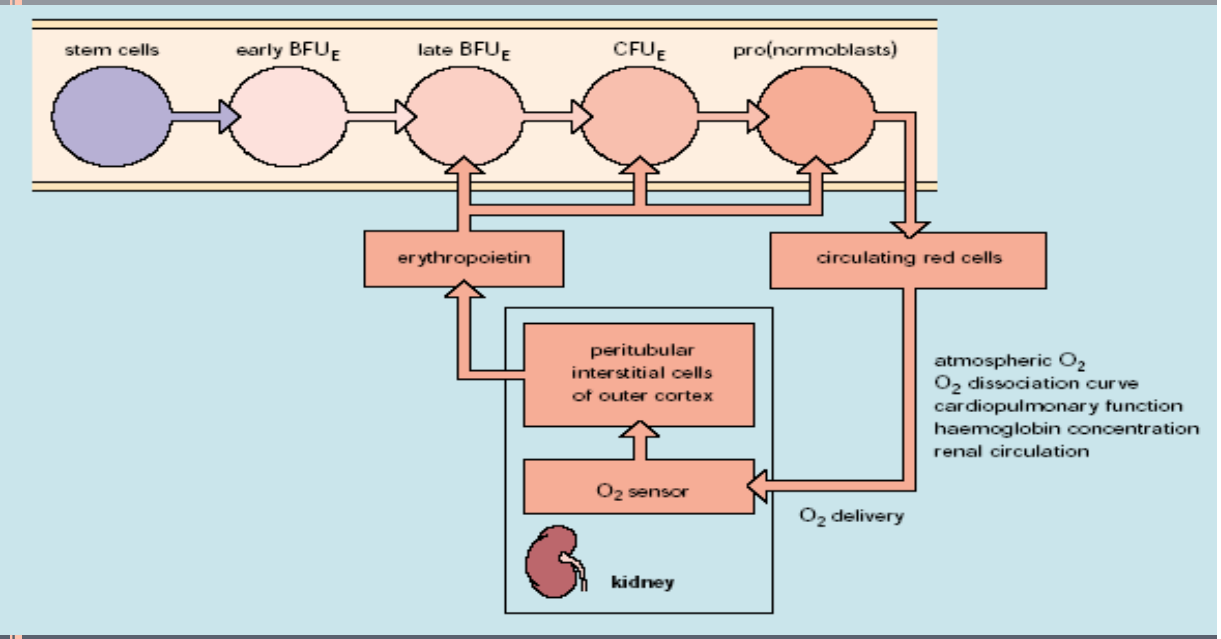
- ❖ the main stimulating factor is hypoxia
- ❑ negative feedback loop that participates in maintenance of normal pO_2 in the blood

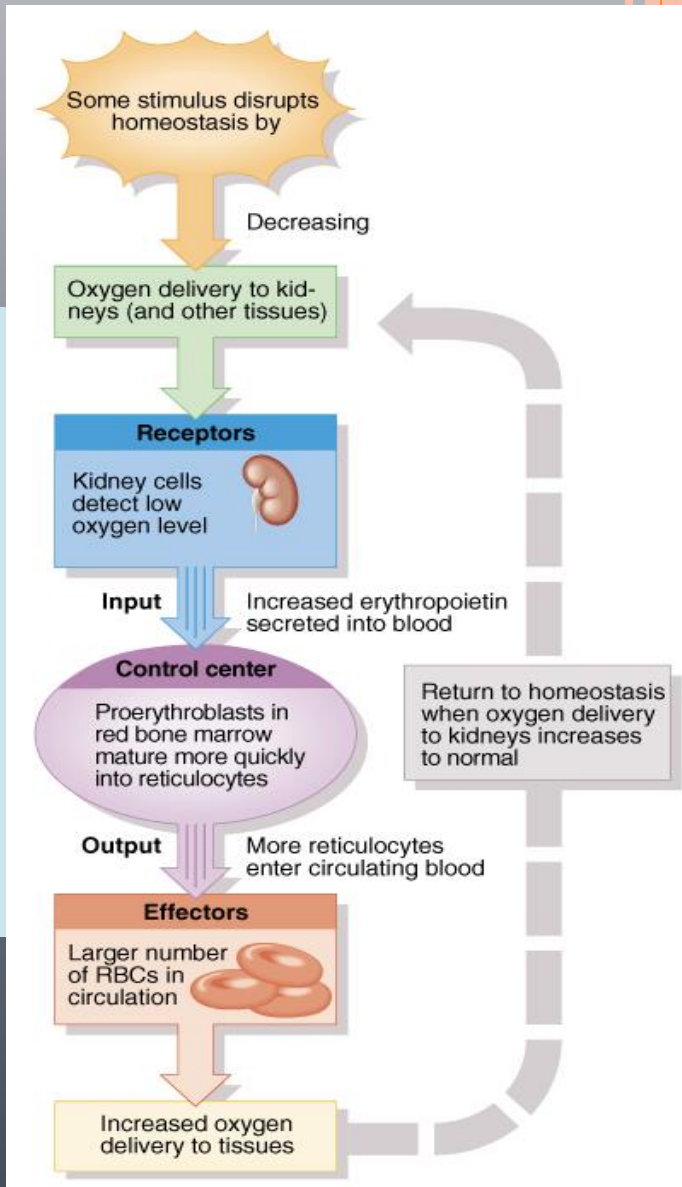


✓synthesis of erythropoietin is stimulated and by the hormones as - testosterone, growth hormone, thyroxin and cateholamines

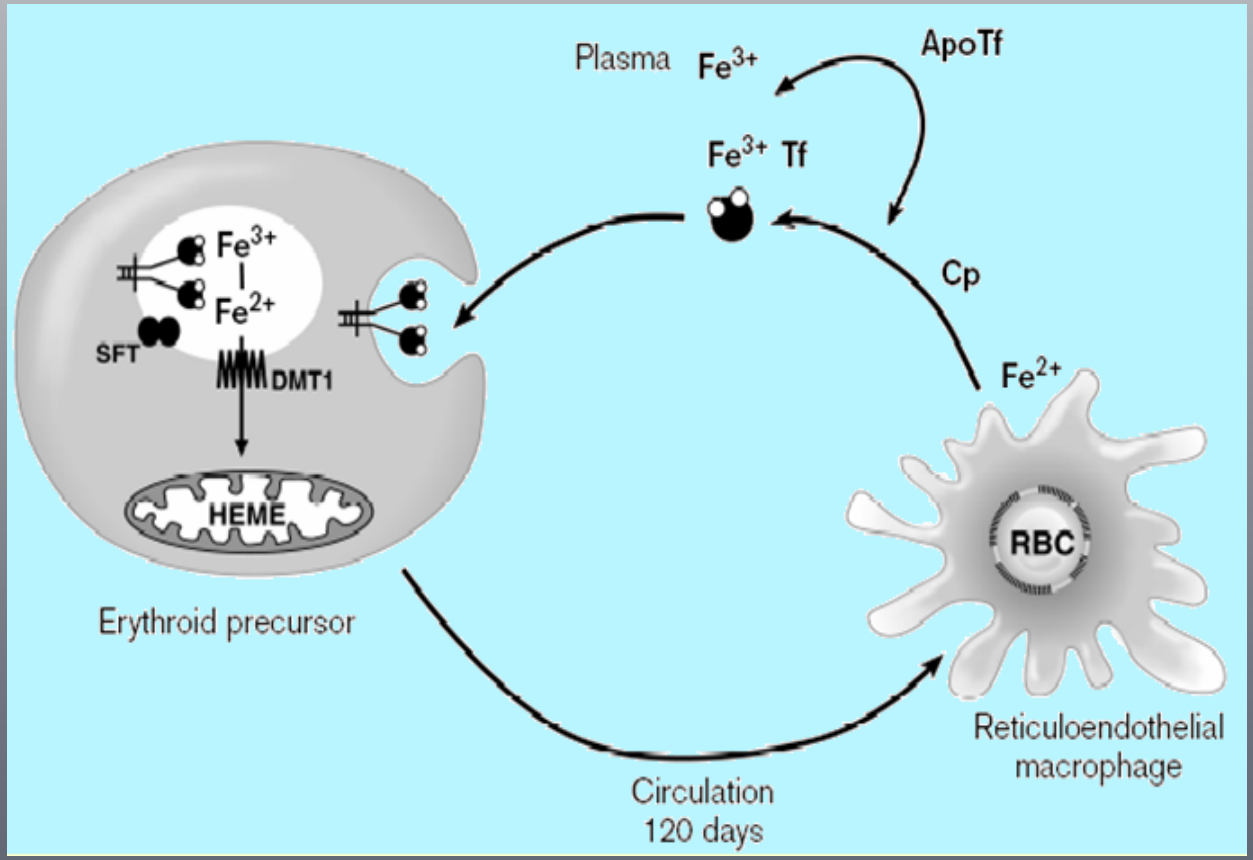
Effects of erythropoietin on bone marrow

✓stimulation of proliferation of early committed progenitor cells (BFU-E, CFU-E)





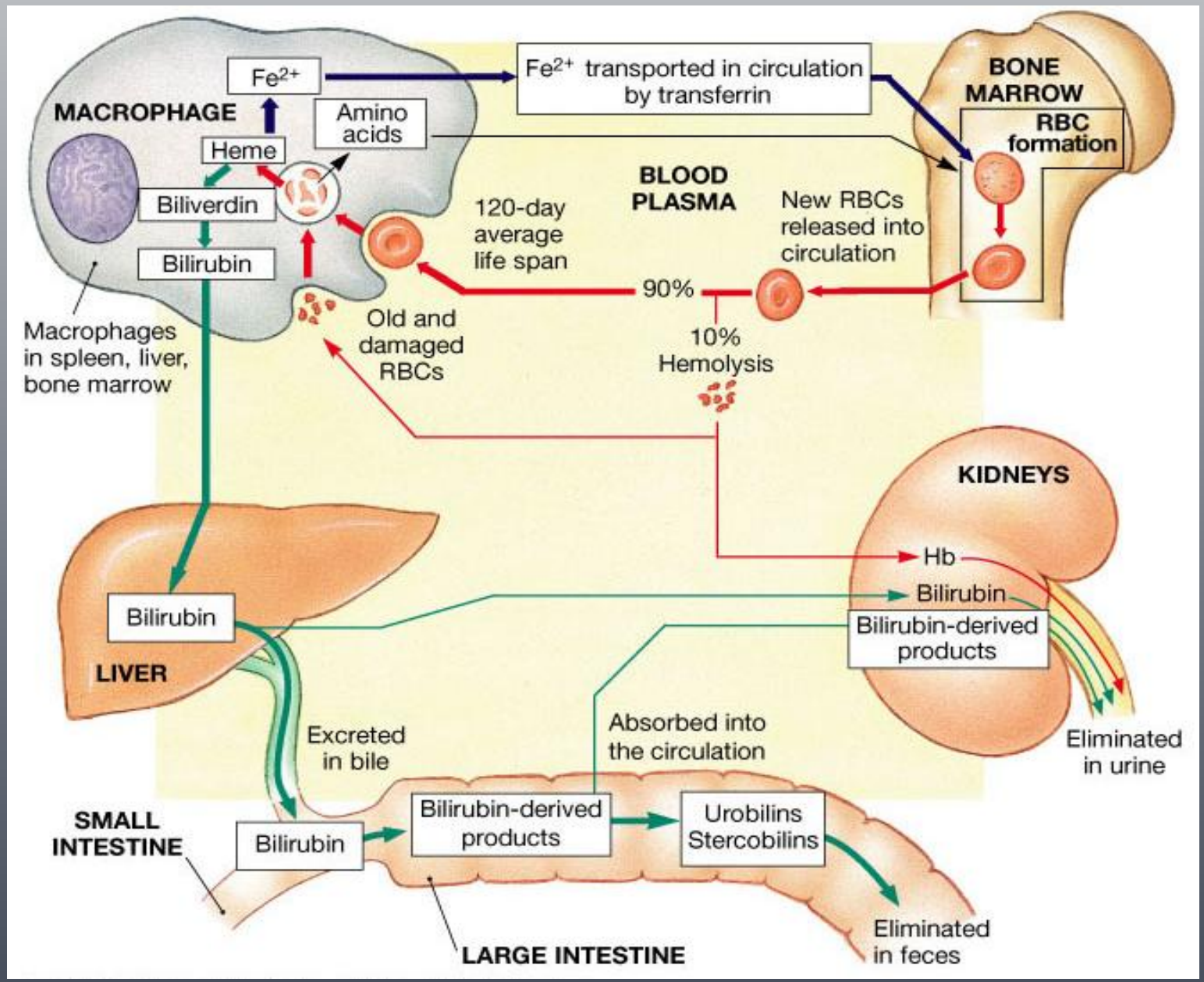
❖ Fe^{2+}, vit B_{12}, folic acid, AA are important for normal erythropoiesis except erythropoietin



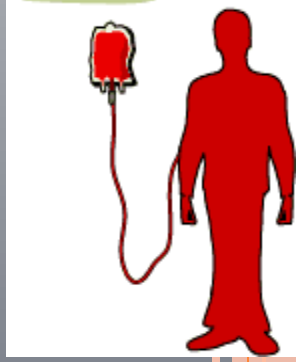
❑ Missing of iron leads to microcytic anemia

➢Vitamin B_{12} and folic acid are important for synthesis of DNA. When they miss –> megaloblastic anemia

Destruction of erythrocytes



Blood groups

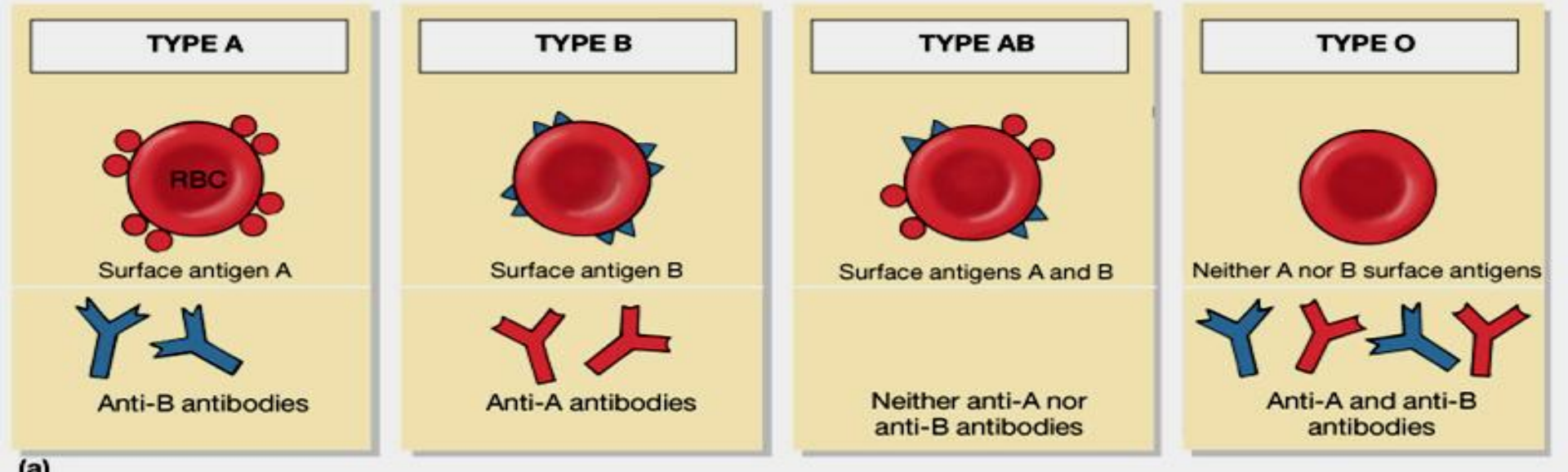


At least 30 commonly occurring antigens and hundreds of other rare antigens, each of them can at times cause antigen-antibody reactions, have been found in human on the surfaces of the cell membranes of RBC.

Two particular types of antigens are much more likely than the others to cause blood transfusion reactions. They are the *O-A-B system of antigens and* the *Rh system*.

ABO System

- ✓2 types agglutinogens- A and B
- ✓2 types agglutinins – anti-A (α) and anti-B (β)
- group A is divided into A_1 and A_2



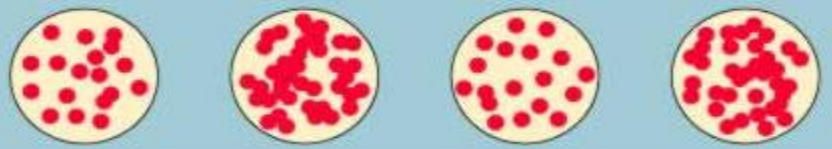
ABO system

Inheritance of blood groups

Blood Group (Phenotype)	Genotypes
O	ii
A	$I^A I^A$ or $I^A i$
B	$I^B I^B$ or $I^B i$
AB	$I^A I^B$

Father's group \ Mother's group	O	A	B	AB
O	O	O, A	O, B	A, B
A	O, A	O, A	O, A, B, AB	A, B, AB
B	O, B	O, A, B, AB	O, B	A, B, AB
AB	A, B	A, B, AB	A, B, AB	A, B, AB

Blood typing

Antibodies Present in Blood	Reaction When Blood from Groups Below Is Mixed with Antibodies from Groups at Left			
	O	A	B	AB
Anti-A Anti-B				
Anti-B				
Anti-A				

Rh system

❖ It is determined by the presence of antigens C, D and E.

➢Antigen D has the highest immunogenity, when it is present the human is Rh(+) , when it is absent - Rh(-).

▪ 85% of white people are Rh(+)

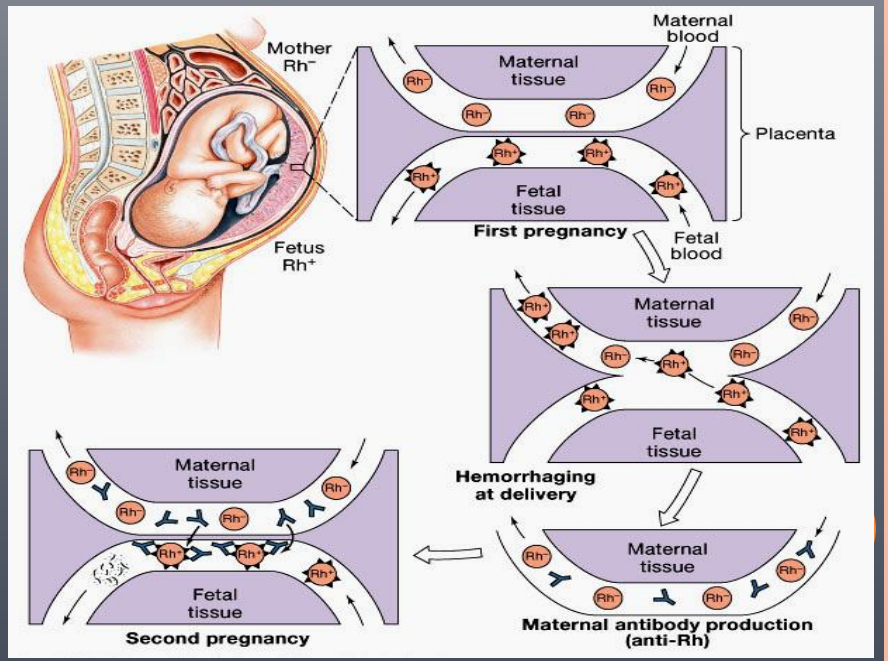
❑Rh(-) people have not anti-D antibodies, but they can produce them when:

✓Rh(-) humane receives Rh(+) blood

✓Rh(-) mother has Rh(+) fetus

During the first pregnancy no danger for the fetus, but after delivery mother may produce anti-D antibodies and the second pegnancy with Rh(+) fetus causes developpment of erythroblastosis fetalis.

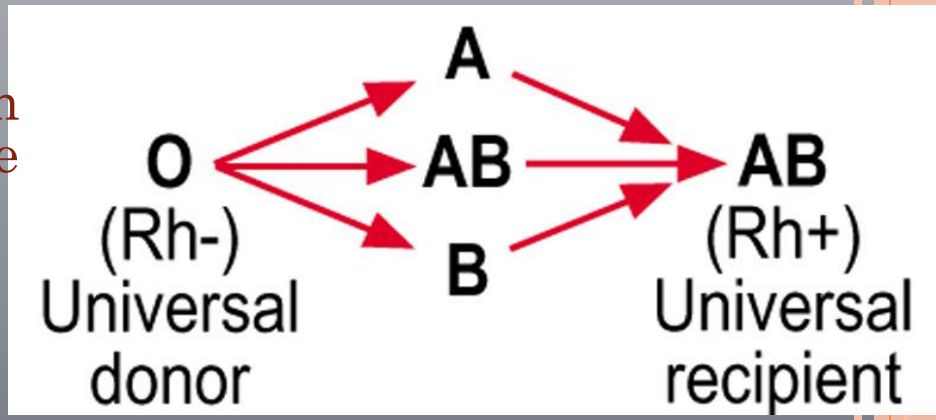
♦ To prevent this reaction after the birth of Rh(+) fetus must inject anti-D immuno-globuline to this Rh(-) woman to activate B Ly and formation of cells of ummunological memory.



The rules for hemotransfusion

❖ ***The erythrocytes of the donor must not be agglutinated by the serum of the recipient.***

➢Group O (α,β) is universal donor, group AB (-) is universal recipient



❑ Autologouse blood may transfuse in unlimited volume, but heterologouse compatible blood no more than 300 ml.

▪ Before hemotransfusion must determine Rh group, Rh (-) patients must receive Rh(-) blood.

> If donor blood of one blood type is transfused into a recipient who has another blood type, a transfusion reaction is likely to occur in which the red blood cells *of the donor blood are agglutinated. Hemolysis of RBC occurs and this leads to death.*