Ministry Of Higher Education and Scientific Research / Al-Mustaqbal University
College of Medical and Health Techniques / Medical Laboratory Techniques Department
Theorotical Hematology / 3rd stage / Dr- Raghda Hameed Jasim M.B.Ch .B-F.I.B.M.S

Lecture two : Hemopoiesis Erythropoiesis and How to control

Haematopoiesis: From Ancient Greek: haima: blood; poiesis to make.

- Is the formation of blood cellular components.
- All cellular blood components are derived from haematopoietic stem cells.
- In a healthy adult person, approximately 10^{11}–10^{12} new blood cells are produced daily in order to maintain blood levels in the peripheral circulation.

Hemopoiesis process includes

- Erythropoiesis: Formation of (RBCs)
- Myelopoiesis: Formation of leukocytes (WBC)
- Megakaryopoiesis : Formation of thrombocytes (platelets)

Site of haematopoiesis:

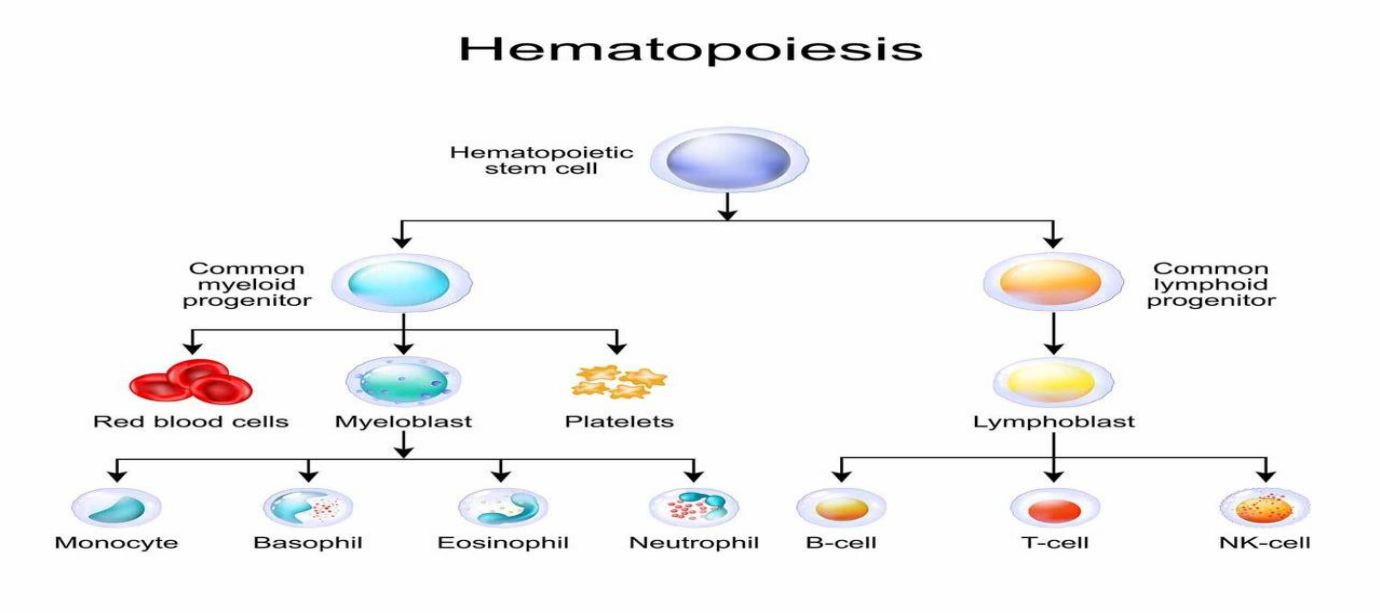
1. Fetus:
- 0-2 months: yolk sac.
- 2-7 months: liver and spleen
- 5-9 months: bone marrow.
2. Infants: Bone marrow (practically all bones).
3. Adults: Vertebrae, ribs, sternum, skull, sacrum and pelvis. Proximal ends of femur and humeri.
4. In the first few weeks of gestation the yolk sac is the main site of haernopoiesis.

Extramedullary haematopoiesis

In some cases, such as some disease, the liver, thymus, and spleen may resume their haematopoietic function , It may cause these organs to increase in size substantially.

The regulation of haemopoiesis : Stem cells are cells from which all hemopoietic elements originate . they are characterized by their ability of self renewal and differentiation .Stem cells require for their proliferation and differentiation

- Certain regulatory factors hemopoietic growth factors
- Suitable microenvironment provided by marrow space
- Stem cells _____ Precursors_____ End stage cells



Erythropoiesis

- The term erythropoiesis (erythro = RBC, and poiesis = to make) used to describe the process of RBC formation or production. In humans, erythropoiesis occurs almost exclusively in the red bone marrow.
- There are approximately 10^{12} new erythrocytes (red cells) each day by the complex and finely regulated process of erythropoiesis.

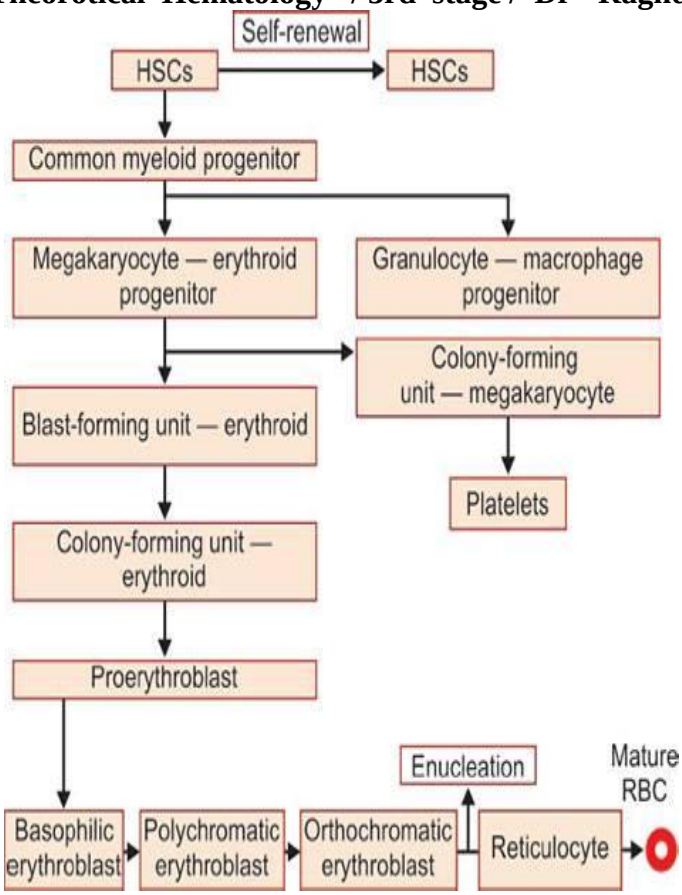
Steps of Erythropoiesis:

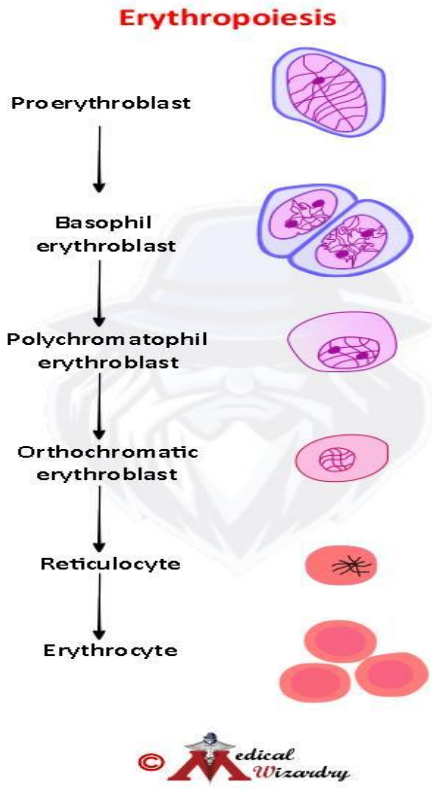
 Erythropoiesis passes from the stem cell through the progenitor cells colony-forming unit granulocyte, erythroid, monocyte and megakaryocyte (CFUGEMM), burst-forming unit erythroid (BFUE) and erythroid CFU (CFUE) to the first recognizable erythrocyte precursor in the bone marrow, the pronormoblast

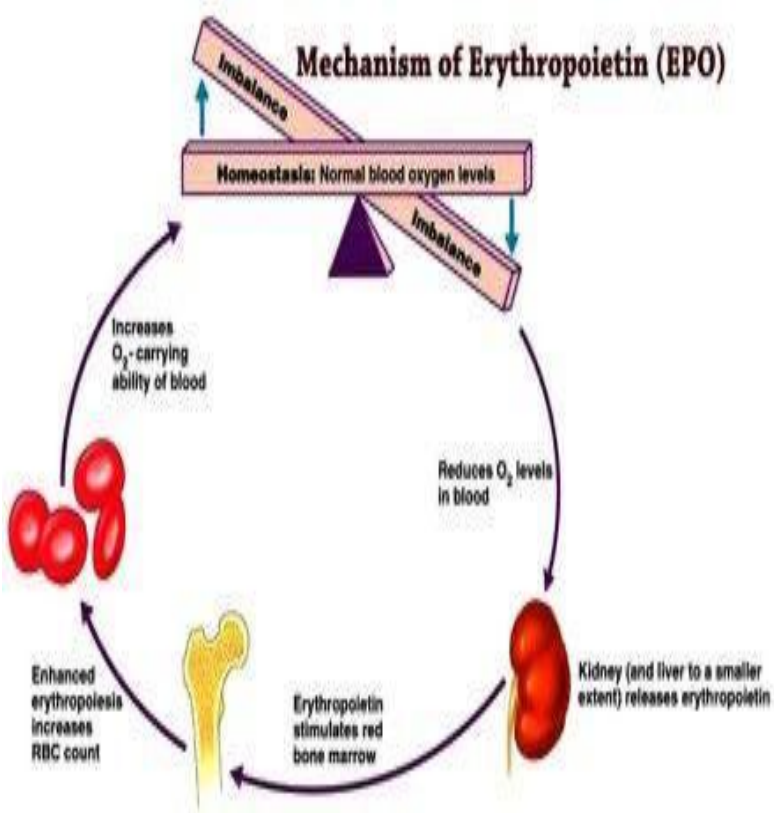
The Mechanism and control of erythropoiesis:

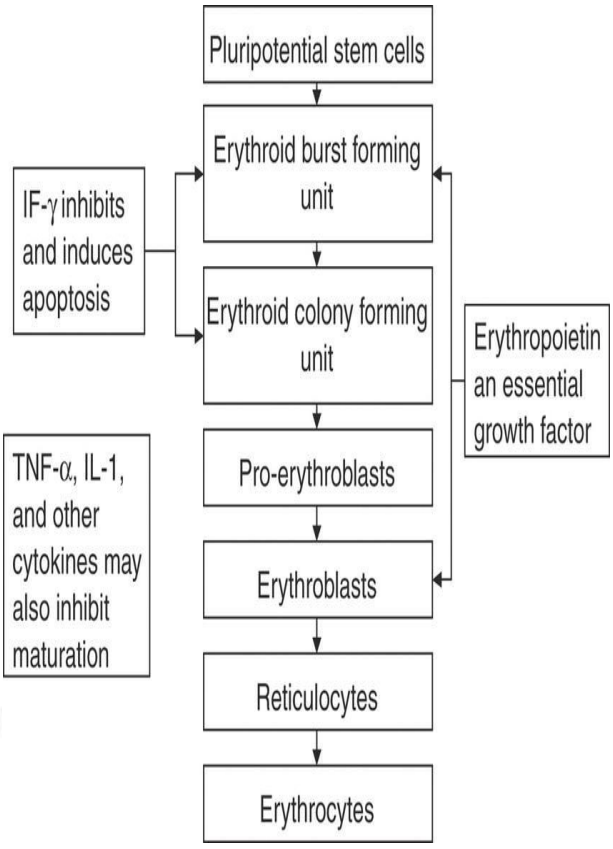
The erythropoietin (formed in kidneys) is released in response to lowered tissue oxygen. Erythropoietin is glycoprotein and stimulates erythropoiesis

It act on the BFU-E (burst-forming units), CFU-E (colony-forming units) and on pronormoblast. Erythropoietin (EPO) interacts directly with the EPO receptor on the red blood cell (RBC) surface, triggering activation of several signal transduction pathways, resulting in the proliferation and terminal differentiation of erythroid precursor cells and providing protection from RBC precursor apoptosis


Self-renewal
HSCs
HSCs
Common myeloid progenitor
Megakaryocyte — erythroid progenitor
Granulocyte — macrophage progenitor
Colony-forming unit — megakaryocyte
Blast-forming unit — erythroid
Platelets
Colony-forming unit — erythroid
Proerythroblast
Enucleation
Mature RBC
Basophilic erythroblast
Polychromatic erythroblast
Orthochromatic erythroblast
Reticulocyte


Erythropoiesis
Proerythroblast
Basophil erythroblast
Polychromatophil erythroblast
Orthochromatic erythroblast
Reticulocyte
Erythrocyte
© Medical Wizardry


Mechanism of Erythropoietin (EPO)
Imbalance
Homeostasis: Normal blood oxygen levels
Imbalance
Increases O2-carrying ability of blood
Reduces O2 levels in blood
Kidney (and liver to a smaller extent) releases erythropoietin
Erythropoietin stimulates red bone marrow
Enhanced erythropoiesis increases RBC count


Pluripotential stem cells
Erythroid burst forming unit
Erythroid colony forming unit
Pro-erythroblasts
Erythroblasts
Reticulocytes
Erythrocytes
IF-γ inhibits and induces apoptosis
TNF-α, IL-1, and other cytokines may also inhibit maturation
Erythropoietin an essential growth factor

Lecture Three : Hemoglobin structure, types, synthesis, levels in blood

Hemoglobin (also spelled haemoglobin and abbreviated Hb or Hgb) is the ironcontaining oxygen-transport metalloprotei

- n in the red blood cells.
- Each molecule of haemoglobin contains four polypeptide (globin) chains and four molecules of haem.
- Globin in adult consist of two alpha (α) chain containing 141 amino acid and two beta (β) chains containing 146 amino acids

Types in humans

:In the embryo

- Gower 1 (δ2ε2)
- Gower 2 (α2ε2)
- Hemoglobin Portland (δ2γ2)

:In the fetus

- Hemoglobin F (α2γ2)

:In adults

- Hemoglobin A (α2β2) - a normal amount 96-98%
- Hemoglobin A2 (α2δ2) - δ chain synthesis begins late in the third trimester and in adults, it has a normal range of 1.5-3.2%
- Hemoglobin F (α2γ2) - In adults Hemoglobin F is restricted to a limited population of red cells called F-cells, it has a normal range of 0.5-0.8%

The level of Hb F can be elevated in persons with sickle-cell disease and thalassemia

Genetics:

Subunit Name	Gene	Chromosomal Locus
Hb α1	HBA1	Chromosome 16 p13.3
Hb α2	HBA2	Chromosome 16 p13.3
Hb β	HBB	Chromosome 11 p15.5

Hb derivatives:

- Oxyhemoglobin
- Deoxyhemoglobin
- Methaemoglobin
- Carboxyhaemoglobin
- Sulfhaemoglobin

Abnormal Hb:

- Thalassemia (β4)
- HbS (α2βS2)
- HbC (α2βC2)
- HbSC

Red Blood Cells (RBCs)Morphology, RBC Function, RBC Structure, RBC Membrane and RBC Metabolism

- Red blood cells are also known as RBCs, red blood corpuscles (an archaic term), erythrocytes (from Greek erythros for "red" and cyte translated as "cell". The term Red Blood Cells is the proper name.
- The color of erythrocytes is due to the heme group of hemoglobin. The blood plasma alone is straw-colored, but the red blood cells change color depending on the state of the hemoglobin:
- when combined with oxygen (oxyhemoglobin) is scarlet.
- when oxygen has been released (deoxyhemoglobin) is darker.

RBCs function: RBCS transport the respiratory gases O2 and Co2

Life Span:

- 120 days, then destroy at RE (reticuloendothelial system) system.
- The important breakdown products are heam and globin that recirculated in the body.
- The heme are broken down into Fe and biliverdin.
- The biliverdin is reduced to bilirubin, which is released into the plasma and recirculated to the liver bound to albumin.
- The iron is released into the plasma to be recirculated by a carrier protein called transferrin. Almost all erythrocytes are removed in this manner from the circulation before they are old enough to hemolyze.

- Hemolyzed hemoglobin is bound to a protein in plasma called haptoglobin which is not excreted by the kidney.

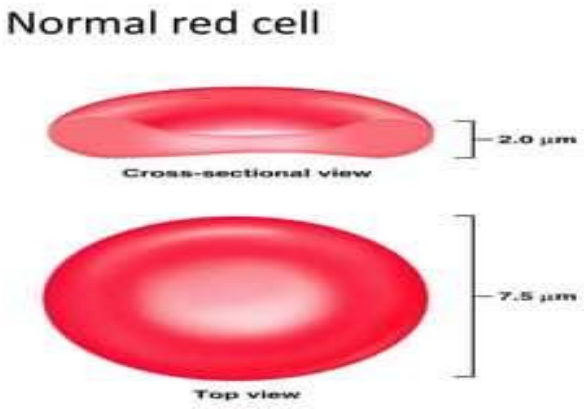
RBCs structure:

- Red cell is structure from cell membrane and cytoplasm filled completely with Hb.
- The RBCs lack the others organelles (nucleus, ribosome, Golgi apparatus and mitochondria.
- Prior to discharge from B.M (bone marrow) into P.B. (peripheral blood) , RBCs shed their nuclei. This gives the advantage:

1. Reduced weight.
2. Transformation into biconcave shape with increased flexibility compared with rigid nucleated cell.

- RBCs is biconcave shape (from side) and spherical (disc) with central pallor from top (⅓ diameter of cell) with 7.5-8 µm in diameter, must be able to pass repeatedly through the microcirculation whose minimum diameter is 3.5-5 µm, in order to:

1. Maintain Hb in reduced 9ferrous Fe++) form.
2. Maintain osmotic equilibrium inside the cell.



RBCs membrane

The red cell membrane comprises a lipid bilayer, integral membrane proteins with surface carbohydrate.

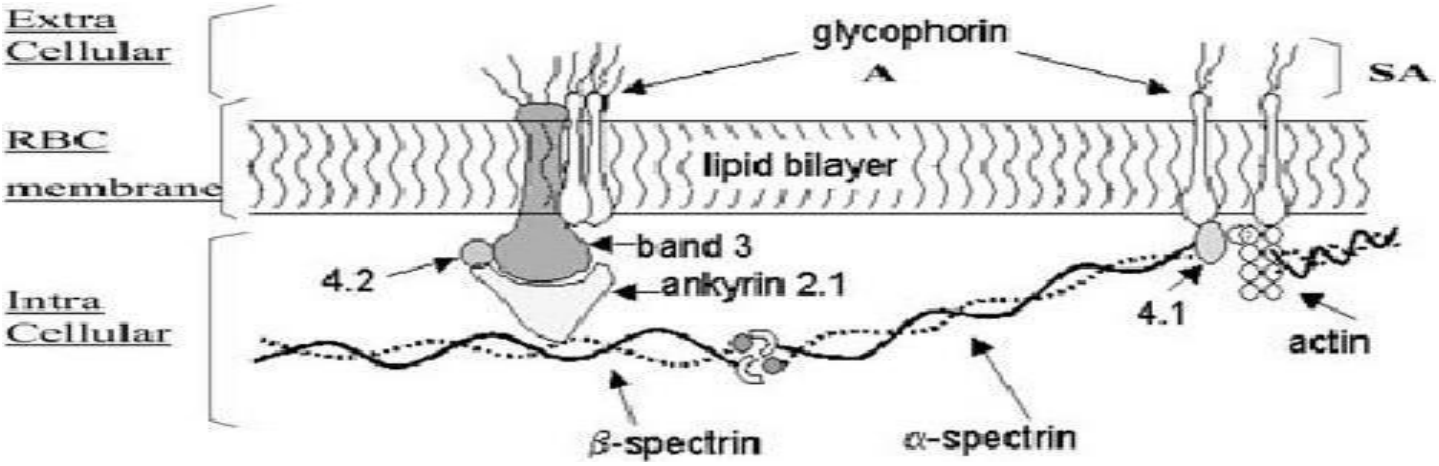
1. 10% carbohydrate : (On the surface , Ags of blood group.)
2. 50% protein : Which include (α and β spectrin , Ankyrin , Protein band 4.1 and 4.2, Actin , Band 3)
   - These protein formed the RBCs skeleton.
   - These protein are important in maintain biconcave shape and transmembrane.

- Any change or defect in these protein may cases some alteration in RBCs shape eg: hereditary spherocytosis and elliptocytosis

3. 40% lipid : (Which include cholesterol and phospholipid)

- Alterations in lipid composition may be associated with others shape abnormalitiis eg:

1. Increase in cholesterol and phospholipid causes target cells formation.
2. Large increase in cholesterol cause acanthocyte formation



RBCs metabolism:

RBCs able to produce energy that required it as:

1. ATP:

- From anaerobic glycolysis (Embden Meyerhof pathway).
- To maintain RBCs shape, volume, flexibility.

2. NADH:

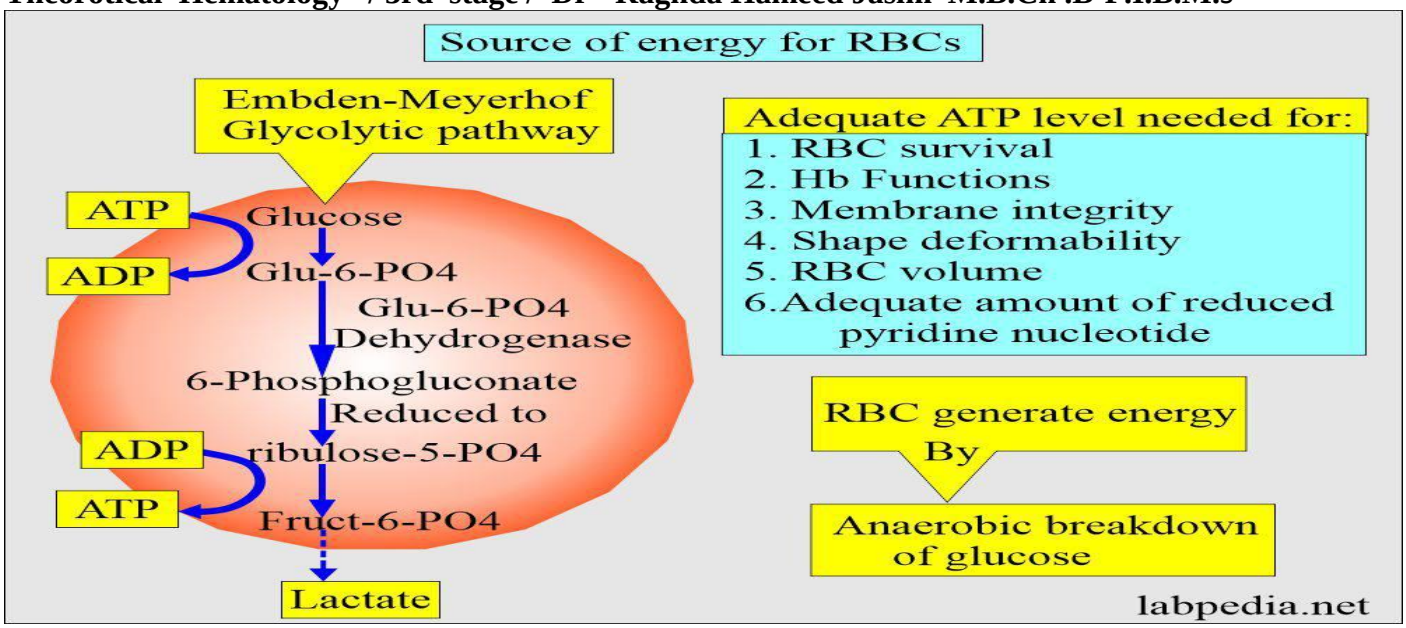
- Also from anaerobic glycolysis
- Reducing power, to maintain Hb in reduced form (reduced met Hb ___normal Hb)

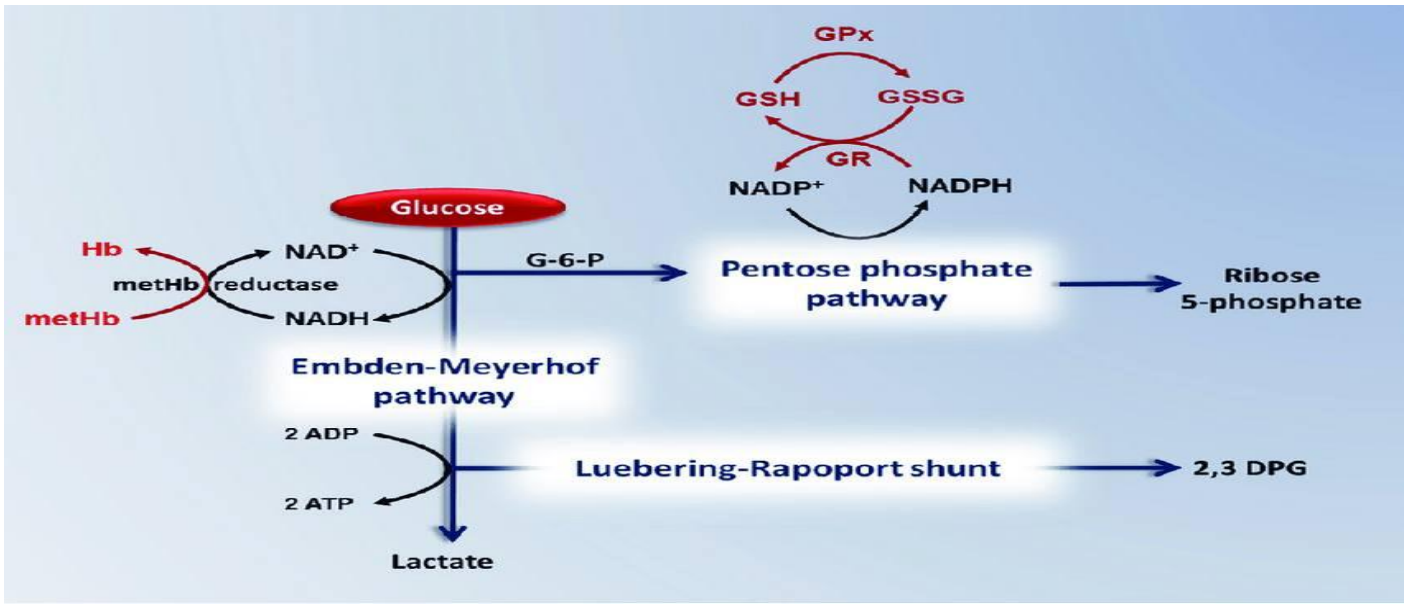
3. NADPH:

- 5% from glycolysis enter HMP (Hexose monophosphate pathway. (
- As NADH also to remove the toxicity from RBCs (antioxidant.(

4. 2,3 DPG (2,3 diphosphoglycerate):

- From Luebering-Rapoport (part from glycolysis)
- Regulation of Hb-oxygen affinity.





The red blood cells diseases include:

- Anemia are diseases characterized by low oxygen transport capacity of the

blood, because of low red cell count or some abnormality of the red blood cells or the hemoglobin.

- Polycythemia are diseases characterized by increase of red blood cells.