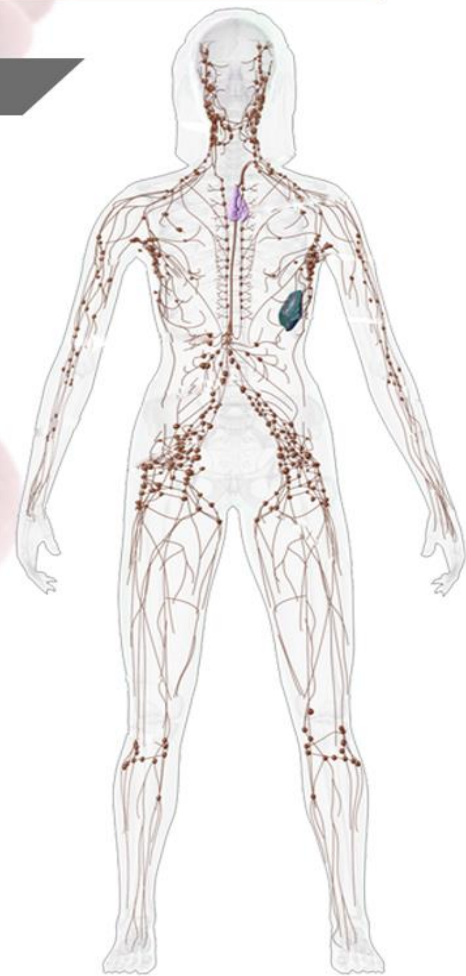
Sheet 2

Hematology and Lymphatic system

Subject | Physiology



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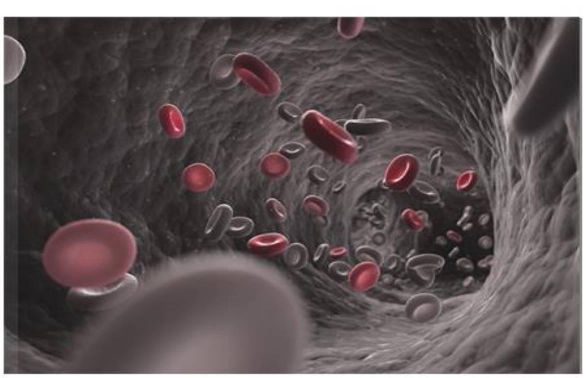
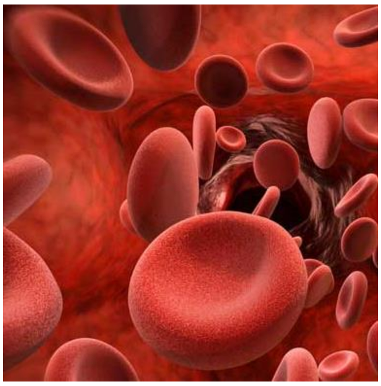


RBCs (Erythrocytes)



- RBCs are circular, **biconcave**, **anucluated** cells. Sometimes minor changes in their shape occur to aid in passing through capillaries. They don't leave capillaries.
- Erythrocytes usually count for: 5 million cell/µL in males and 4.5 million cell/µL in females → 5 million cell/µL in humankind in general.
- **Corpuscular** is another name of RBCs.
- µL= micro liter, is the **most common** used unit for RBC count.

Dimensions of RBCs:

1- **MCV** (mean corpuscular/cell volume): it is the most important parameter, which is a measure of the average **volume of red blood cells**. The usual normal range is (**80-90**) μm^3 OR fL. It might be lower than that reaching (78-79) and or higher reaching (91-92) which is normal.

fL (femtoliter) = μm^3 (micron cubic).

2- **Surface area**: normal range 132-138 μm^2.

3- **Diameter**: 7.5-7.8 µm.

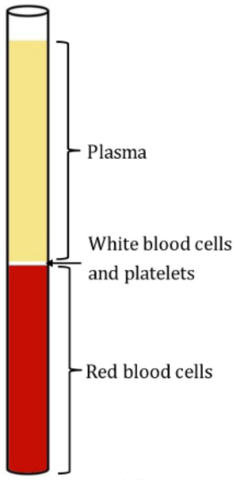
- MCV is elevated or decreased in accordance with the other red cell dimensions; surface area and the diameter.

a When viewed in a standard blood smear, RBCs appear as two-dimensional objects, because they are flattened against the surface of the slide.

b The three-dimensional shape of RBCs.

c A sectional view of a mature RBC, showing the normal ranges for its dimensions.

Blood Parameters



1- **RBCs count:** actual number of RBCs within a given blood sample.

2- **Hematocrit (Hct):** percentage of the **volume of red cells** relative to the **total blood volume**. It can be measured by the following equation:

$$Hematocrit = \frac{Height\ of\ the\ RBCs\ column}{Height\ of\ the\ total\ blood\ column}$$

The shape of RBCs are **not uniform**, they are biconcave desks, and therefore, around **2%** of plasma is **trapped** within the RBCs in the tube.

It has been shown that hematocrit tests gives values approx. 2 % too high due to plasma trapped in the RBC layer.

3- **Hemoglobin content (Hgb):** measures the **amount** of oxygen-carrying protein (**hemoglobin**) in the blood

- In new-born babies all three parameters of blood are higher than in normal adults. This happens due to:

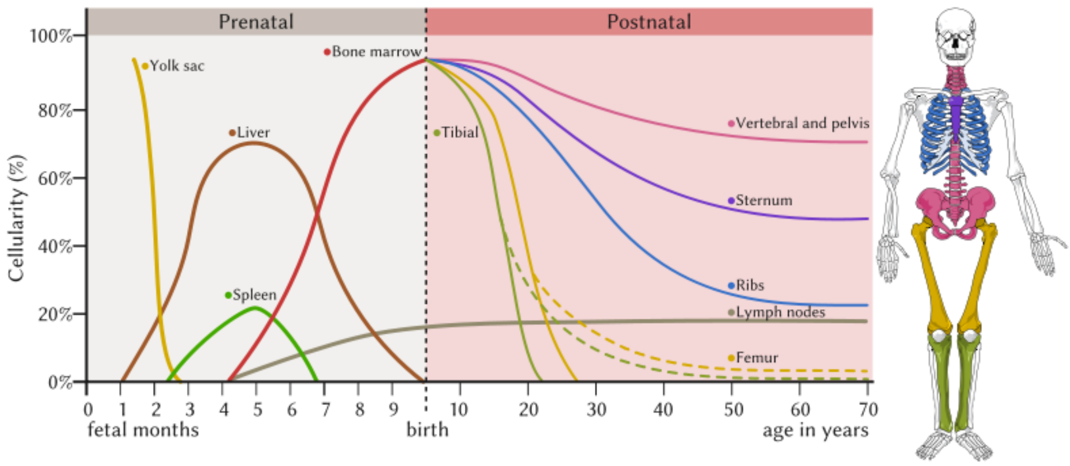
  a- **Fetal oxygenation** will shift from placental oxygenation into pulmonary oxygenation after birth; breathing through oneself lungs.

  b- **Fetal hemoglobin** will later turn into adult hemoglobin.

  ⇨ When fetal oxygenation and fetal hemoglobin turn into pulmonary oxygenation and adult hemoglobin respectively during their 7th month after birth, blood parameters are normalized.

Blood Cells Production

- **Hematopoiesis** is the formation of **all** blood cells, while **Erythropoiesis** is formation of mainly **RBCs**. Both processes are vital to keep the number of circulating blood cells within their normal range.



a- In fetal life (prenatal), erythropoiesis occurs during the first 2 months mainly in the **yolk sac**, then in the **liver**, and to a lesser extent, in the **spleen**.

b- At the beginning of the 5th month, the **bone marrow** (primarily) and the **lymph nodes** are responsible for erythropoiesis.

c- After birth the **bone marrow** is the only site for production of blood cells.

d- During childhood bone marrow of **all bones** produce blood cells.

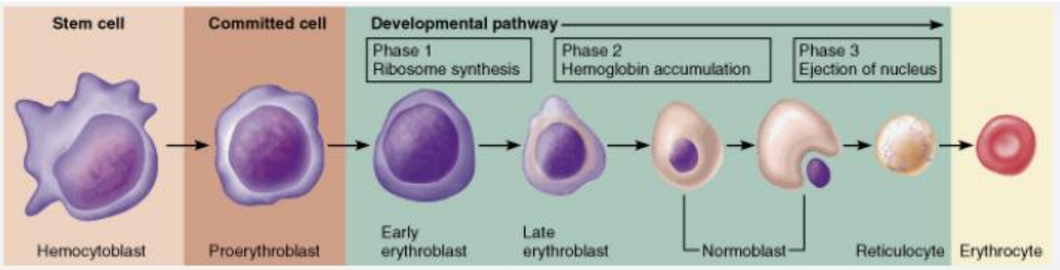
e- At the age of 18 in females and 20 in males (adulthood) blood cell production is **limited** to some bone marrow found in the vertebrae, pelvis, sternum, ribs, and especially the ends of long bones like the femur, tibia, ulna, and radius, as well as the scapula and the clavicle.

(The order is important)

⇨ **In summary:** During the prenatal period: yolk sac → liver → spleen. At the 5th month: bone marrow and lymph nodes. After birth: only bone marrow of all bones is responsible. At adulthood: limited to some bones marrows.

Erythropoiesis Stages:

- Erythrocyte differentiation takes place in 8 stages. It is the pathway through which an erythrocyte matures from a **hemocytoblast** into an **erythrocyte**. The first seven stages all take place within the **bone marrow**. After stage 7 the cell is released into the **bloodstream** as a **reticulocyte**, where it then matures into an erythrocyte.



- During erythropoiesis, **Erythroblasts** mature into **Normoblasts**. In the **last** stage, **Reticulocytes** are generated in the **bone marrow** from **Normoblasts** by **enucleation**.
  After (2-3 days) in the bone marrow, reticulocytes are released into **circulation**, where they **eliminate** their residual **RNA**, all internal membrane-bound organelles, and **ribosomes** (1-2 days) maturing into **erythrocytes**.

  *i.e. **Reticulocytes** are cells that have **lost** their nucleus but still **retain** residual **RNA**. Their development **begins** with the **extrusion** of the **normoblast** nucleus and **ends** when the reticulocyte has **lost** its **organelles** maturing into an **Erythrocyte** in the circulation.*

- The number of reticulocytes in the circulation is **less** than their number in the bone marrow.
- If Reticulocytes make up 1-2% of RBCs then erythropoiesis is normal, below that means erythropoiesis is low.
- In the bone marrow: the number of reticulocytes = the number of **nucleated** cells (erythroblast cells).
- In **hemolytic anemia**, the reticulocyte percentage is **high**, with **low RBC** count (abnormal condition).
- Up until stage 7, **hemoglobin** is being synthesized. Mature Erythrocytes (RBCs) contain **no nucleus** and thus hemoglobin synthesis doesn't occur there.

Regulation of erythropoiesis:

Factors that regulate RBCs and keep their number relatively constant and normal are **oxygen supply, dietary vitamins supply 'B12', and iron.**

1- **Oxygen supply**: when the amount of **oxygen decreases** (hypoxia) the number of **RBCs increases** to compensate for this reduction by transporting O_2. When the amount of oxygen increases, which occurs among people who live around the sea level, RBCs count becomes lower.

Hypoxia can be caused by low blood volume, anemia, low hemoglobin, poor blood flow, and pulmonary diseases. Low O_2 levels **does not** directly affect the **blood marrow**; it affects the cells in the **kidneys** which sense oxygen levels, and when oxygen levels are low these cells produces **erythropoietin** which **stimulates erythropoiesis**.

Note: Erythropoietin is a **glycoprotein hormone** that enhances the production of RBCs by affecting erythrocyte stem cells until hypoxia is relieved. It **promotes** the formation of red blood cells by the bone marrow.

- Half-life: 10 hours.
- 90% is produced by the **kidney** and 10% by the liver and a very little amount is produced by the spleen if any.
- It is traceable in both plasma and urine.
- The duration of erythropoietin activity is 3-6 days and is functional for 6 hours.

2- **Dietary vitamins supply:** All vitamins play a role in erythropoiesis, mainly B12 (essential), Folate (essential), Vitamin C (involved in every process in the body).

a- Vitamin B12:

- Also known as extrinsic factor, cyanocobalamin, and maturation factor. It is obtained from our diet.
- In the stomach it combines with the **intrinsic factor** produced by the stomach cells. This complex moves toward the lower **ileum** where it is absorbed into the circulation and either participates in the **erythropoiesis** (bone marrow) or is **stored** in the liver.
- B12 is essential for many functions:

  a- DNA formation.
  b- Normal function of myelin sheathes in the CNS. In the case of B12 deficiency myelin sheath cannot conduct nerve impulses.
  c- Maturation of RBCs.

Vitamin B12 deficiency:

- Vitamin b12 deficiency reduces the **production of RBCs** leading to one type of anemia called **megaloblastic anemia** (pernicious anemia).
- **Neutrophils** are also affected by the deficiencies of vitamin B12.
- Vitamin B12 is needed for RBCs maturation, thus a deficiency affects the maturation (prolonged to over 6-7 days). However, hemoglobin **synthesis** stays normal, therefore, **RBCs** count is **low** while the hemoglobin content is relatively **high**.

- The cells produced because of the deficiency of vitamin B12 are **larger** than normal and oval in shape, leading to **MCV** to be relatively **high** (above 110 and might reach 160 μm^3 instead of 80).
- Anemia means a low amount of hemoglobin. So even though the volume of the cells increases, the number of RBCs **decreases**, further decreasing the number of cells that **retain** hemoglobin. This is what causes the **anemia**.
- 2-3 mg of vitamin b12 is sufficient for normal body function for almost 2-4 years. Therefore; anemia due to b12 deficiency in the diet is **very rare**.

Causes of vitamin B12 deficiency:

1- **Veganism** (people who do not eat meat or other animal-based products).
2- **Malabsorption**:
   a- **Gastric causes** → Congenital lack of intrinsic factor // Partial or total gastrectomy.
   b- **Intestinal causes** → Chronic tropical sprue (diarrhea) // Ileal resection.

b- Folic Acid:

- Folic acid is also a maturation factor for RBC, thus its deficiency causes **megaloblastic anemia**. It has **no role** in myelin sheath formation whatsoever unlike Vit. B12.
- The deficiency of folic acid produces cells similar to the cells produced by the deficiency of vitamin B12.
- The **jejunum** has an enzyme that facilitates the absorption of the folic acid.

Causes of Folate deficiency:

1- Inadequate dietary intake b.
2- Malabsorption: Celiac disease // jejunal resection // tropical sprue.
3- Pregnancy.
4- Premature infant.
5- Chronic hemolytic anemia.

Definite effects of vitamin B12 or folate deficiency:

1- Megaloblastic anemia.
2- Macrocytosis of epithelial cell surface.
3- Neuropathy (B12 deficiency only).
4- Sterility in severe anemia.
5- Rarely reversible melanin skin pigmentation.

Good Luck