Sheet No. 2

Physiology

Hematolymphatic System

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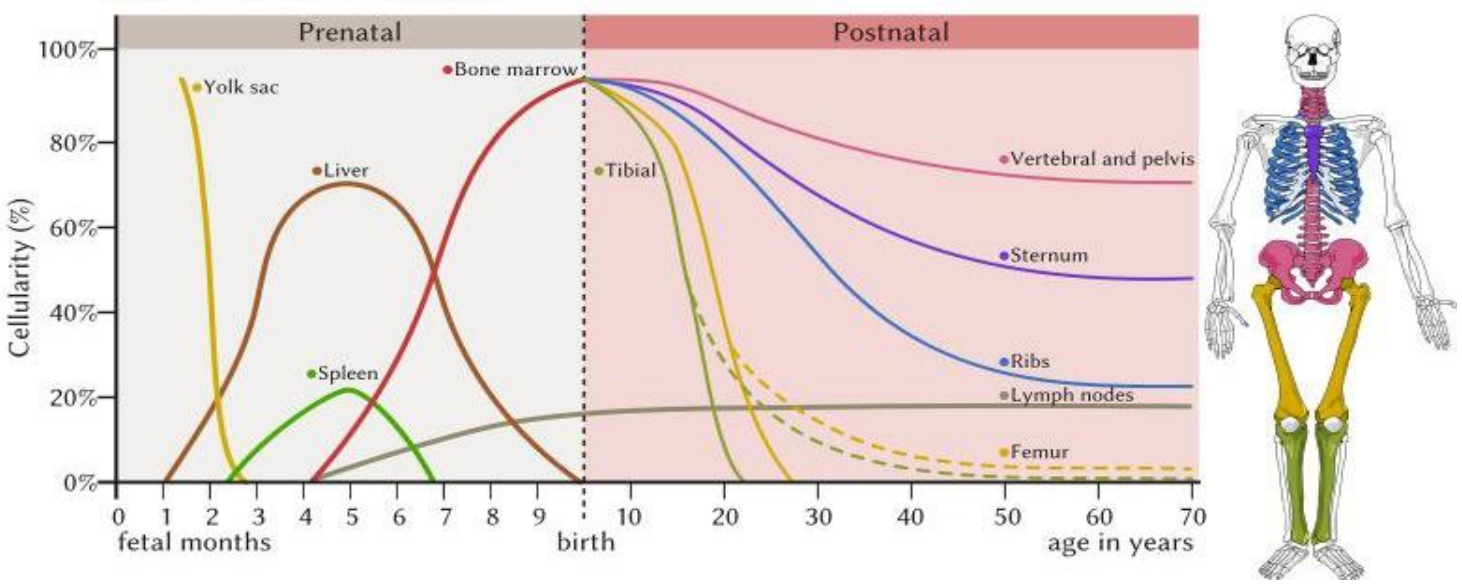
1.Erythropoiesis

The half-life of RBCs is 120 days and after this period these cells will be destroyed and replaced by new cells by a process called erythropoiesis.

So, Erythropoiesis or hematopoiesis is the process by which red blood cells (erythrocytes) are produced.



→As you can see, before birth (during fetal months) blood cells are produced in the yolk sac during the first two months. After that, and until birth, they are produced mainly in the liver, with little production by the spleen. At the beginning of the 5th month, the bone marrow and lymph nodes start producing blood cells.

→ After birth, erythropoiesis occurs only in the bone marrow and lymph nodes will stop producing RBCs. Before reaching 18-20 years, erythropoiesis takes place in the marrow of all bones, but after the age of 20 RBCs formation is confined to some bones only (Vertebra and pelvis, sternum, ribs, femur and tibia).

(In the 020 lecture the doctor said ➔after the age of 20, RBCs formation is confined to the vertebra, pelvis, sternum, ribs, skull, ends of long bones, scapula and clavicle)

→Note: This is what normally happens, and what SHOULD happen. However, in some abnormal cases, RBC production can continue in the liver and Spleen after birth

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The successive appearance of the different forms of blood cells:

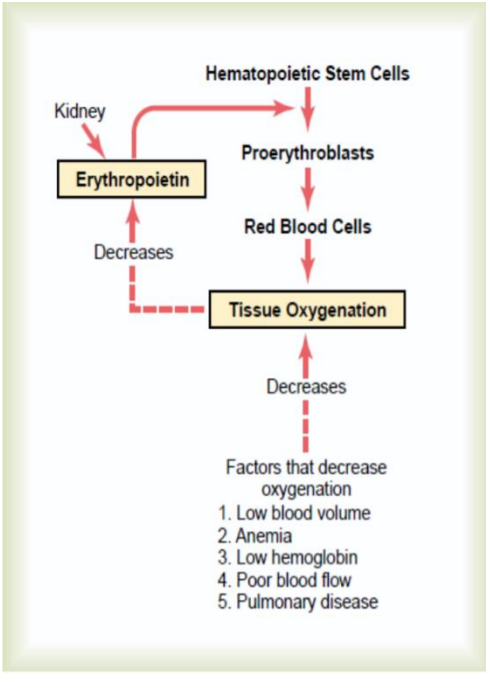
Primitive erythrocytes➔ definitive erythrocytes & megakaryocytes ➔granulocytes

➔lymphocytes ➔monocytes

2-Regulation of erythropoiesis:

Normally, the number of blood cells -whatever type- remains constant in specific concentrations in the blood. We can say that **production of blood cells = destruction.** This process is regulated by several factors including:

- **Oxygen supply:** when the amount of oxygen decreases (hypoxia) the number of RBCs increases to compensate for this reduction by transporting O2. When the amount of oxygen increases, which occurs among people who live around the sea level, RBCs count becomes lower



→ In this figure we can see that low tissue oxygenation, which has many causes, stimulates cells in the kidney to produce **erythropoietin** which in turn stimulates RBCs production.

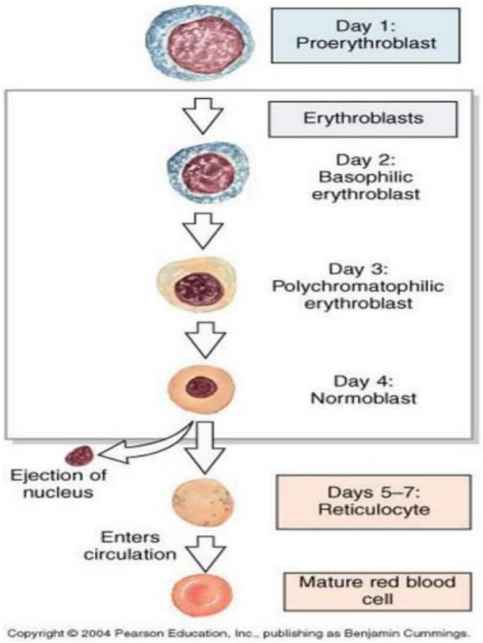
→*Erythropoietin is a glycoprotein hormone that enhances the production of RBCs by affecting erythrocyte stem cells until hypoxia is relieved. It promotes the formation of red blood cells by the bone marrow.*

- 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.

Clinical information (that has nothing to do with our topic):
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, any % 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).

*We will talk more about this in histology



- Hemoglobin synthesis continues throughout all stages of maturation but mature RBCs and peripheral reticulocytes are devoid of RNA and can no longer synthesize hemoglobin.

- **Dietary vitamins supply:** All vitamins play a role in erythropoiesis, mainly B12, Folate, and Vitamin C.
  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 other than maturation of RBCs, like DNA formation and normal function of myelin sheaths in the CNS. In the case of B12 deficiency, myelin sheath cannot conduct nerve impulses.

***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 while there is deficiency of vitamin B12 are larger than normal and oval in shape. As a consequence, MCV tends to be relatively high (above 100 and might reach 150 μm^3). and have short half-life

- Even though the volume of the cells increases, the number of RBCs decreases, further decreasing the number of cells that retain hemoglobin.

- 2-3 mg of vitamin B12 is sufficient for normal body function for almost 3-4 years. Therefore, anemia due to B12 deficiency in the diet is very rare. (Some findings suggest that it can be due to a deficiency in intrinsic factor)

*** 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 (carboxypeptidase) that facilitates the absorption of folic acid.

***Causes of Folate deficiency:**

1- Inadequate dietary intake

2- Malabsorption: Celiac disease, jejunal resection, tropical sprue.

3- Increased requirements: Pregnancy, premature infant, 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.

Short Quiz

1- Fetal erythropoiesis occurs in the liver from …. To ….?

a- Second month / death

b- Second month / birth

c- First month / second month

d- During the whole fetal life

2- A 15-year-old boy on a vegetarian diet presented with pale skin, dizziness and fatigue. Lab findings were (hemoglobin, 5.1 g/dL; mean corpuscular volume, 116 fL). This kid most probably suffers from:

a- Liver problems

b- Anemia of B12 deficiency

c- Pernicious anemia

d- More than one of the above

3- If the reticulocyte percentage is higher than 1% but RBCs count is quite low you suspect:

a- Hemolytic anemia

b- Bone marrow suppression

c- A mutation in erythropoietin

d- None of the above

4- An old woman with severe kidney disease (her kidney is ischemic and almost non-functional) lives on high altitude where pO2 is quite low. She will most likely have:

a- High reticulocytes percentage

b- Anemia

c- Over-stimulation of erythropoietin but everything else is fine

d- None of the above

Answers

1. b
2. d
3. a
4. b

Good Luck!!