In this lecture we will talk about

- Some characteristics of RBC .
- Erythrpoiesis :

  * During fetal & adult life.

  * its regulation .

RBCs :

- Appear under the microscope as circular ,unnucleated and biconcave shaped cells .
- Can change their shape (in order to pass narrow blood vessels) .
- Don't leave the blood vessels (if it leave it this indicate an abnormal condition) .
- Dimensions of RBC :

  There are 3 important dimensions:

  1. MCV (mean cell volume) normally ranging from 80 to 90 FL .
  2. Surface area (135±16 μm^2) .
  3. diameter (7.82± 0.5 µm) .

     There are other dimensions such as maximum thickness and the minimum thickness these two dimension change according to MCV .

-the main function of RBC: Transporting of O_2 and CO2 and keeping Hb inside it .

* imagine if the Hb is free (e.g. hemolysis) in the plasma what happens?

a. Colloid osmotic pressure will increase b. Viscosity of the blood will increase c. The load on the heart will also increase .

- The count of RBC in males = 5 million ; while in females 4 million per microliter .

a. Erythrocytes constitute 45% of the blood .

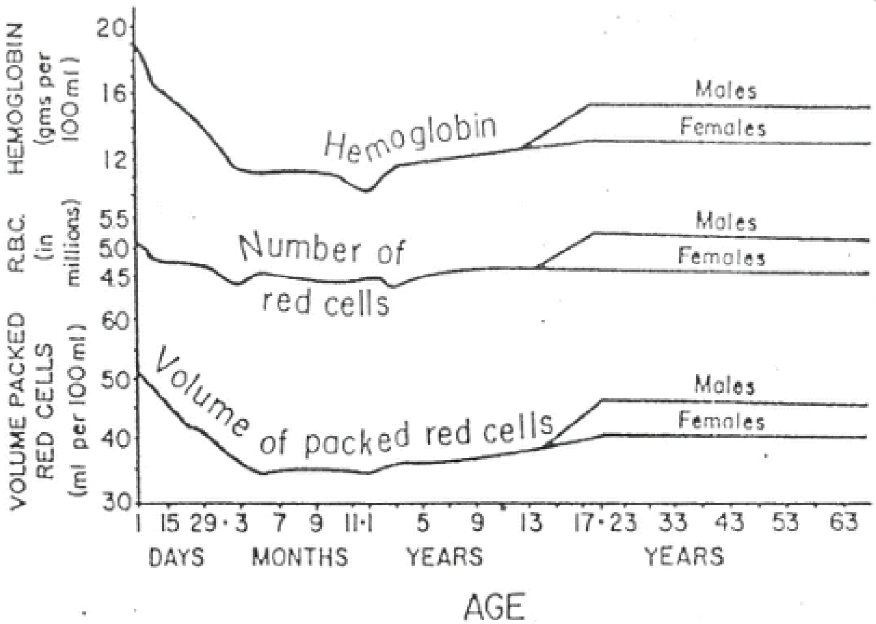
* If we take a tube full of anti-coagulated blood and we centrifuge it , we will find that - 55% of the blood is plasma .

b. Less than 1% Buffy coats leukocytes & platelets .

c. 45% erythrocyte (we call the 45% of the erythrocyte "hematocrit", also we call it HCT & packed cell volume (PCV) .

(If you remember the RBCs aren't uniform in shape , they are biconcave disk shape, therefore; they trap in between it some plasma this plasma is called trapped plasma. About 2-3% of the plasma is found in between RBC) .

- Relation of age to Hb content, RBC count and hematocrit of the blood



- In new born & the fetus specially in the last stage ; the PCV , RBC count & Hb are higher because the oxygenation is restricted to placenta & because of the fetal Hb , within 2-3 months after birth the parameter will return to normal .

(PCV& RBC count return to normal) because of free oxygenation & shifting of the fetal Hb to adult Hb.

<u>Erythropoiesis</u>: (hematopoiesis)

Is the production of RBCs .

Sites of blood erthropoiesis in fetus and after birth .

We can see

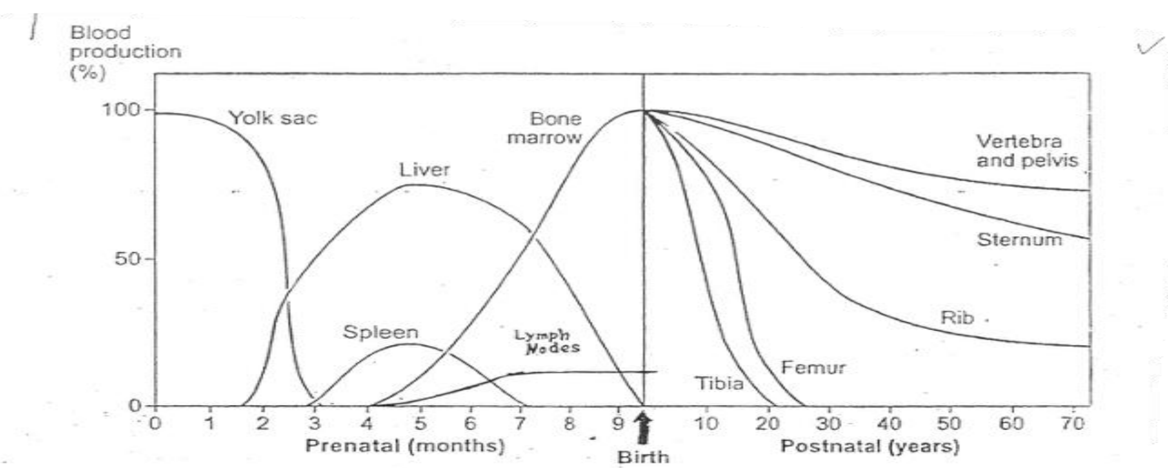


Fig. 1 Sites of blood production in the fetus and after birth. (Erythropoiesis)

in this figure that:

- **in the fetal life**

A. the erythropoiesis mainly occurs in the liver (2nd month till birth) .

B. at the beginning of fetal life erythropoiesis occurs in the yolk sac .

C. in the spleen erythropoiesis occurs from the 4^{th} to 8^{th} month but very little in compared to liver.

D. erythropoiesis takes place in the bone marrow at the beginning of the 5^{th} month .

E. erythropoiesis also takes place in the lymph nodes but little amount .

After birth erythropoiesis only remains in bone marrow of all bone till age (18-20) years old , after that the erythropoiesis confined to some areas.

(Mainly to vertebrae, pelvis, sternum, ribs, skull & the ending of long bone as femur and tibia) .

<u>Note:</u> the active bone marrow is called red bone marrow while the inactive is called yellow bone marrow.

* The successive appearance of different form of blood cells:

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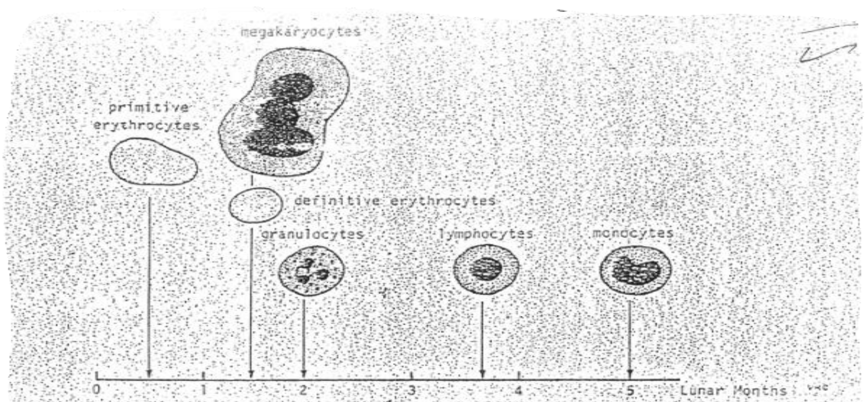

Fig. 17-6. The successive appearance of the different forms of blood cells.

- At the beginning (first month) just RBCs are produced (primitive erythrocyte) .
After one month megakaryocytes are produced then granulocyte then lymphocyte and at the beginning of the 5^{th} month monocytes are produced .
- So we can see that during fetal life not all blood cells are produced immediately; its produce one by one .
- The number of the blood cells or RBCs is kept relatively constant (Because the # of RBCs are produced= to # of RBCs that are destroyed) .

***** There are many factors that keep the number of circulating RBCs constant:

1st factor oxygen supply

In hypoxia ⟶ erythropoiesis increases .
While in hyperoxia ⟶ erythropoiesis decreases (such as in people live around Dead Sea level) .

*****How does hypoxia increase the erythropoiesis?

There are cells in the kidney (glomeral apparatus) these cells are sensitive to low O_2 level. So in low O_2 level this cells produce erythropoietin, erythropoietin affects hematopoietic cell to continue producing RBCs.

*****Causes of hypoxia: low blood volume, anemia, low Hb, poor blood flow, pulmonary disease

*There are two sources of erythropoietin (glycoprotein hormone) :-

- renal (90% of erythropoietin is produced in kidney) .
- extrarenal (10% of erythropoietin is produced in the liver & spleen) .

*note : erythropoietin half life is 6 hours .

*****Erythropoitic activity range from (3-6) days (less than 3 days is abnormal, also more than 6 days is abnormal)
At the end of erythropoiesis the reticulocyte are produced (this cell has rudimentary fragments of the nucleus and it synthesizes Hb) .
The reticulocytes are found in the bone marrow (remain 2-3 days) and also in circulating blood .
*just about 2% of reticulocytes are found in circulating blood at normal condition
More than 2% ⟶ indicates hyperactivity
Less than 2% ⟶ indicates hypoactivity
*No Hb synthesis in the mature RBC .

2nd factor is vitamins

1. Vit B_{12} also called cobalamine & extrinsic factor

-**Function of vit B_{12}:** it is essential for the formation of DNA and it is essential for normal function of myelin sheath in the nervous system .

-**How we get vit B_{12}**?

Vit B_{12} ingested with food when it reach the stomach it will bind with the intrinsic factor (to protect it from digestion) then this complex goes down to lower ileum to be absorbed by receptors then vit **B_{12}** either participate in erythropoiesis or goes to the liver to be stored in .

-Vit B_{12} deficiency produces anemia called pernicious anemia (megaloblastic anemia) .

-**How the vit B_{12} deficiency produces anemia?**

Deficiency of vit B_{12} leads to DNA formation problem (the time of DNA formation will prolong which leads to cell growth without division) while the hemoglobin synthesis is normal .

-**The Result of vit B_{12} deficiency**: RBC count is reduced but the cells are larger than normal, containing more amount of Hb, oval in shape & they have shorter half life .

-**Causes of vit B12 deficiency**:

a. Food related is very rare because 2-3 mg is sufficient for human being for about (3-4) years .

b. Problem in production of intrinsic factor (the main cause) .

*note : all the vitamins play a role in erythropoiesis especially vit. C and vit. B12 .

2. Folic acid deficiency very similar to vit B_{12} deficiency but is less severe than vit B_{12} deficiency .

***Causes of folic acid deficiency:** inadequate dietary intake, malabsorbtion (e.g. , celiac diseases , jejunal resection , tropical spure) , increase requirement .

folic acid is absorbed in the jejunum .

Folic acid deficiency also **causes** low count, lager with high Hb RBCs .

Folic acid deficiency causes megaloblastic anemia .

3rd factor Iron:

- 4-5 g iron in our body .
- Iron is presented in nature in two forms ferric (Fe^{+3}) form and ferrous form (Fe^{+2}) we benefit from the ferrous form .
- We take iron in the food daily "15-20 mg" but we benefit only 4% of this ingested iron .

Sources of Iron

- food

*in food iron is present in the ferric form as it reach the stomach it will be converted into ferrous form by the effect of HCl then iron bind with transferrin that is produced from the epithelial cell --> then transferrin remains on the surface and ferrous transfer to the epithelial cells --> bind with ferritin --> to carriers --> to carry iron into the circulation --> then iron either participate in erythropoiesis or goes to the liver to be stored.

*There're enzymes in the epithelial cells which separates iron from Hb .

*It is mostly absorbed in the duodenum (and as we get distally in the intestine the absorption decrease ; very little in the colon) No absorption in the stomach .

- heme

- Myogloulin

***Daily requirement of iron:**

Table 2.3 Estimated daily iron requirements. Units are mg/day.

	Urine, sweat, faeces	Menses	Pregnancy	Growth	Total
Adult male	0.5–1				0.5–1
Post-menopausal female					
Menstruating female*	0.5–1	0.5–1			1–2
Pregnant female*	0.5–1		1–2		1.5–3.0
Children (average)	0.5			0.6	1
Female (age 12–15)*	0.5–1	0.5–1		0.6	1–2.5

- Female, pregnant female & female age (12-15) are most likely to develop iron deficiency if they don’t take supplement .

The table below represents iron absorption favoring factor and reducing factor :-

Table 2.2 Iron absorption.

Factors favouring	Factors reducing
1 Ferrous form	1 Ferric form
2 Inorganic iron	2 Organic iron
3 Acids—HCl, vitamin C	3 Alkalis—antacids, pancreatic secretions
4 Solubilising agents—e.g. sugars, amino acids	4 Precipitating agents—phytates, phosphates
5 Iron deficiency	5 Iron excess
6 Increased erythropoiesis	6 Decreased erythropoiesis
7 Pregnancy	7 Infection
8 Primary haemachromatosis	8 Tea
	9 Desferrioxamine

* **Distribution of iron in the body:**

Iron is mainly distribute in Hb (65%) , ferritin and haemosiderin (30%) , myoglobin (3.5%) , heme enzyme (0.5%) , transferrin (0.1%) .

***Causes of iron deficiency**:

a. Blood loss as peptic ulcer ,..etc (not menstruation) .
b. Increase in demand (prematurity , growth and child-bearing) .
c. Malabsorption .
d. Poor diet .

Iron deficiency:

- hypochromic microcytic (also Sideroblastic anemia which is failure of protoporphyrin syntheis or problem in globins' synthesis ; all of the three are hypochomic microcytic) .
- Iron deficiency is a universal condition which is estimated to affect about 30% of the world population.
- Iron deficiency anemia is still the most important deficiency related to malnutrition .
- Iron deficiency anemia (IDA) and thalassemia trait (TT) are the most common forms of microcytic anemia .
- Iron deficiency anemia is a common clinical problem in both developing and industrialized .
- Some discrimination indices calculated from red blood cells indices are defined and used for rapid discrimination btw IDA &TT .

The End

Sorry for any mistake & good luck ^^

Done by:
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