

Human Physiology

Lecture 3 – Wednesday 17/2/2016

“Structure, production and function of erythrocytes” with

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PharmaGlory 15

The book is “Essentials of Physiology”/”Fundamentals of Physiology” by Sherwood.

Note: RBC= Red Blood Cell, WBC = White Blood Cell
[B] = from the book, not the lecture.

- Reminder: blood is composed of two parts: a fluid part (plasma) and the formed elements (RBCs, WBCs, platelets).

The major formed element is the RBCs/**erythrocyte**.

- RBCs
 - are **disc-shaped cells**,
 - Have a diameter of 8 micrometers (μm).
 - and no nucleus
- Major function of RBCs is the transport of O_2 by Hemoglobin from the lungs to the tissues. RBCs also transport CO_2 by Hemoglobin.
- RBCs contain a large amount of **carbonic anhydrase** – an enzyme that catalyzes (speeds up) the conversion of H_2CO_3 into Hydrogen (part 2) and bicarbonate ions as follows:

(Part 1): $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3$ (carbonic acid: acids destroy the formed elements.)

(Part 2) $\text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-$ (bicarbonate ions are more soluble in water).

So carbonic anhydrase helps with the acid-base balance in the cell.

>هذا الإنزيم يحافظ على توازن الحموضة في الخلية. عندما يدخل ثاني أكسيد الكربون خلية دم حمراء، يقوم بالتفاعل مع المياه و ينتج حمض الكربونيك. هذا الحمض يدمر الخلية، لكن الإنزيم المذكور يحفز تفكيك الحمض إلى أيونات البيكربونات (و هذه الايونات تذاب بسهولة في الماء)<

- ± 3.5 million per kg per day of RBCs is produced in our body.

In males: 5 million

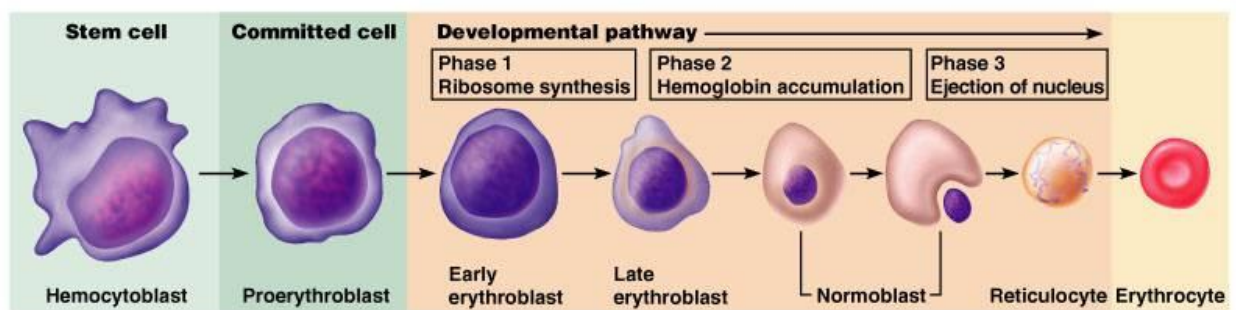
Females: about 4 million

At birth (newborns): about 5.5 million.

The difference between males & females is due to the male sex hormone (testosterone) as it effects the red bone marrow, causing it to make more RBCs.

In newborns, there is less O_2 available for them when they're inside the uterus (الرحم), causing their body to produce more RBCs.

- The life of an RBC is about 120 days. After that, it gets destroyed.
- The production of RBCs, called **erythropoiesis**, happens in the red bone marrow.
- The formed elements (RBCs, white blood cells, and platelets) all originate from the same cell – a stem cell that is found inside the bone marrow. So when RBCs are inside the bone marrow, they still have a nucleus. The picture below shows how RBCs originated from a stem cell, and how they had a nucleus before they specialized to form an RBC.



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فائدة الصورة: لتوضيح الفكرة، بأن خلايا الدم الحمراء أتت من خلايا جذعية و كانت تحتوي على نواة. لا داعي للحفظ.

- Bone marrow that is surrounded by fat cells is called **yellow bone marrow**.

- Blood -> RBC -> Hemoglobin -> Iron

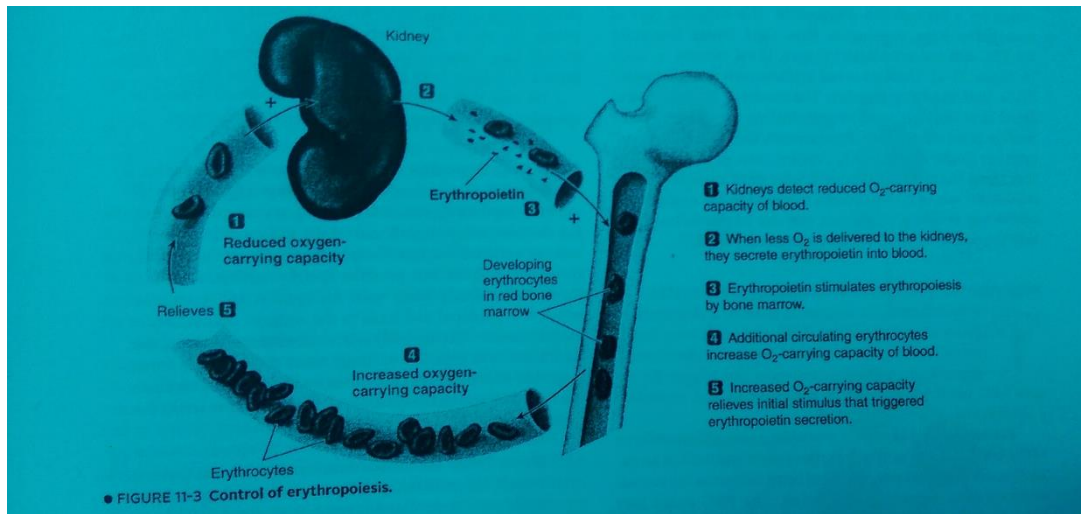
The major function of blood/RBC/hemoglobin/iron inside the hemoglobin is transport of O₂.

- Reminder: **Hypoxia** is a decrease in the amount of O₂ that stimulates the production of RBCs. There are many types of Hypoxia, but in general Hypoxia means a decrease in the amount of O₂.

Important note: A decrease in the number/concentration of RBCs does NOT cause RBC production. ONLY the decrease in amount of O₂ does.

>إنتاج خلايا الدم الحمراء لا يعتمد على قلة خلايا الدم الموجودة... فقط على قلة نسبة الأوكسجين في الدم <

- **Production of RBCs:**



- Hypoxia causes special cells in the kidney to release **Renal Erythropoietic Factors (REF)**. Hypoxia also affects the liver, causing it to release Globulin (a plasma protein).
- REF & Globulin combine to form a glycoprotein (بروتين سكري) hormone called **Erythropoietin** hormone.
- Erythropoietin enters the circulation & causes the red bone marrow to produce RBCs.

- **Polycythemia** is an increase in the amount of RBCs or “Hematocrit”, above the normal amount.
- If the amount of O₂ is normal, but there is a decrease in the amount of Hemoglobin, and this causes **iron-deficiency anemia** (Note: there are many types of anemia).
- So: Increase in RBCs -> Polycythemia
Decrease in Hemoglobin -> Anemia
- To make a red blood cell we need:
 - Protein (to form hemoglobin)
 - Erythropoietin
 - Iron
 - Vitamin B12 & Folic acid.

- Vitamin B12 is found in animal products (cheese, meat, etc.)
Vitamin B12 is very important for the formation of RBCs and DNA.
In order for Vitamin B12 to be absorbed, we need the **intrinsic** factors (عوامل داخلية) in the stomach. In the duodenum (first part of small intestine), the Vitamin combines with the intrinsic factors in order to be absorbed.

A deficiency or lack of Vitamin B12 causes anemia ([B]: another type of anemia called **Pernicious anemia**).

Note: So the problem is not in the lack of Vitamin B12, but rather in lack of intrinsic factors.

- A deficiency in Vitamin B12 causes:
 - Cells become larger than normal
 - Cells develop an irregular shape (not a disc-shaped cell anymore)
 - Cells having a shorter life (because of the irregular shape. The cells with an irregular shape will be destroyed by special cells in the spleen (طحال))
- Every RBC has about 300 million hemoglobin molecules.
 Each molecule of hemoglobin has 4 Iron atoms.
 Every atom of Iron can bind with 1 molecule of O₂.
- Each 100 ml of normal blood has about 15g of Hb (the number is different in males from females).
 Each gram of Hb can transport about 1.34 mL of O₂.
 So 100mL of blood can transport 20.1mL (15*1.34) of O₂.
- Hemoglobin is made of two parts: Heme groups & globin.
 Heme is the iron-containing part of the Hemoglobin.
 [B]: Globin is the protein part, made of 4 polypeptide chains... the four iron-containing, nonprotein groups are called heme groups.
 Hemoglobin is a blood protein, not a plasma protein.
- Hemoglobin can combine with:
 - CO₂ – Carbon Dioxide [reversible], transported from the tissues back to the lungs.
 - O₂ – Oxygen [reversible], transported from the lungs to the tissues.
 - H⁺– Hydrogen Ions[reversible], transported from the reaction we discussed before that takes place in the RBC:

$$\text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-$$

- CO – Carbon Monoxide [irreversible]. Hemoglobin can bind with CO 250 times faster than O₂. CO is produced by cigarette smoke. This is why smokers have a higher concentration of Hb than non-smokers, because they have more non-functional Hb (Hb that combined with CO).

>التدخين ينتج أول اكسيد الكربون. عندما يدخل أول اكسيد الكربون دم الإنسان، يقوم بالتفاعل مع الهيموقلوبين. يقوم أول أكسيد الكربون بالتفاعل مع الهيموقلوبين ٢٥٠ أسرع من الأوكسجين، لذلك نسبة الهيموقلوبين عند المدخنين أعلى (حتى تعوض عن الهيموقلوبين المعطل)<

- NO – Nitric Oxide [reversible] – vasodilator ([B]: NO relaxes and dilates (توسيع) the arterioles (الشرايين). It is useful to stabilize blood pressure.
- Meaning of “reversible”: It can be stopped/removed/replaced. Meaning O₂ can be removed or replaced by CO₂. But Hb that has combined with CO results in a permanent (دائم)

Note: Some of the details of this lecture are found in Chapter 11 (The Blood and Body Defenses), pages 319 to 322