Hematology

PHYSIOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number: 4

Subject: Hb, PO_2 and others

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Price:

بسم الله الرحمن الرحيم

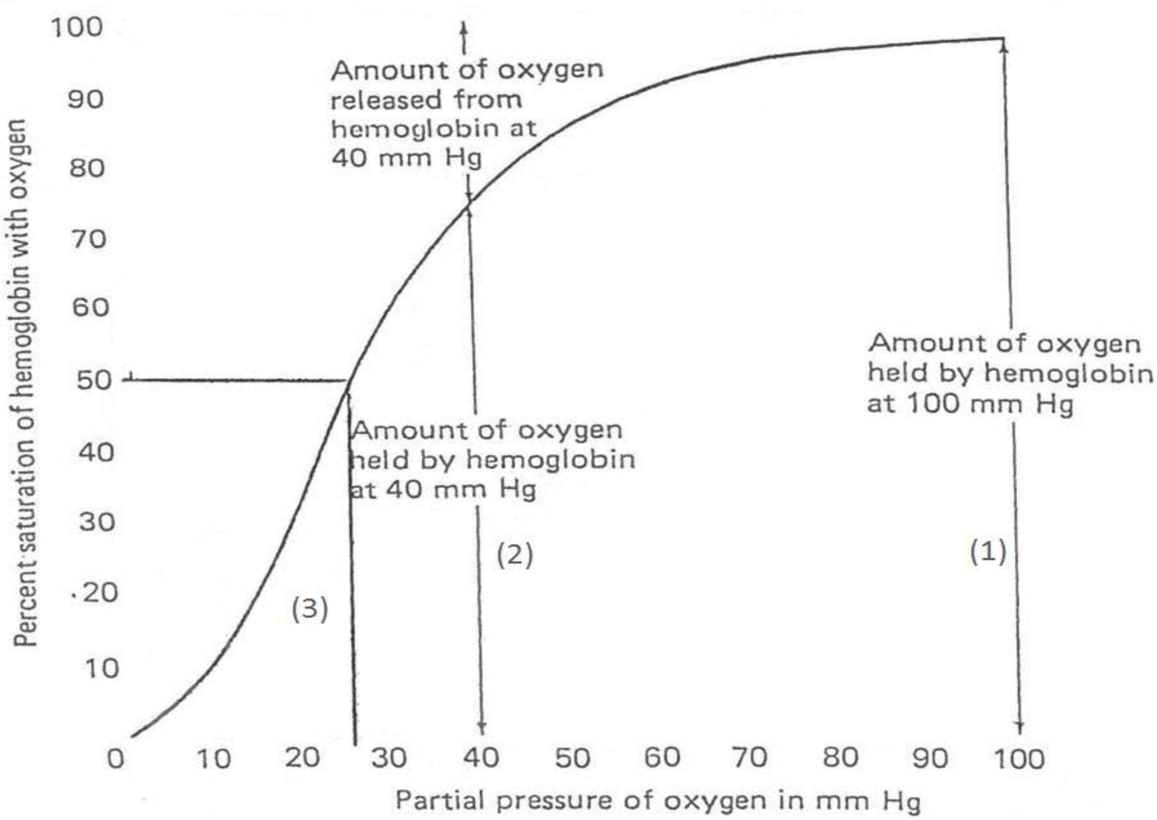
- This sheet was written according to the recording of section 2.
- Things written in *Italic* were not mentioned during the lecture. READ THEM to understand.

➢ Points discussed in the last lectures :
    - Hemoglobin concentration in males is 16g/100ml blood.
    - Hemoglobin concentration in females is 14g/100ml blood.
    - When the sex isn't specified, hemoglobin concentration is estimated to be 15g/100ml blood.
    - RBC count :
      Males → about 5 million cells/mm^3 blood.
      Females → about 4 million cells/mm^3 blood.

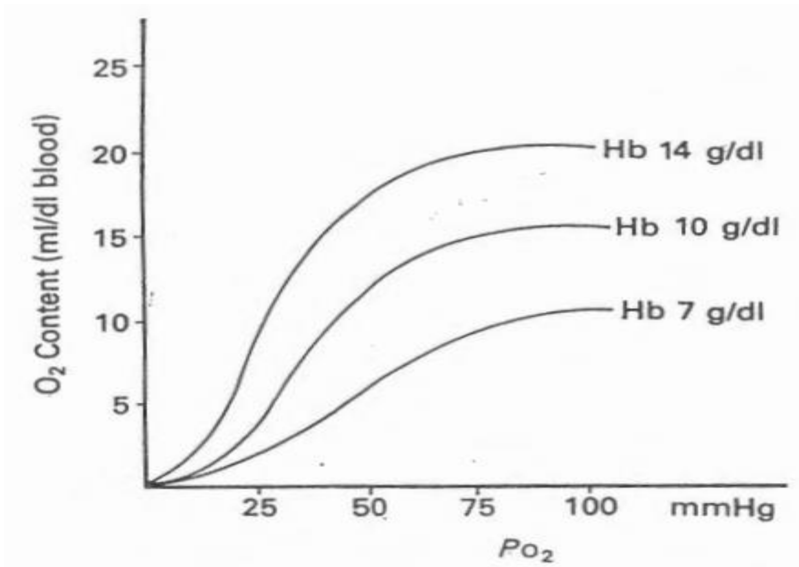
    - Hemoglobin molecules contain:
      1. A protein part, Globin (96%) → binds to CO_2, hydrogen ion, 2,3-DPG, and many other substances.
      2. A Ferrous containing heme part (4%) → binds oxygen only.

➢ **Plasma and the whole blood are brought into equilibrium (same PO_2), which means they have the same amount of dissolved oxygen. However, the oxygen content of the whole blood is much higher than that of the plasma because of the binding of oxygen to hemoglobin in RBCs.**
    - 1 gram of hemoglobin binds 1.34 ml of oxygen. Therefore, 100 ml of blood carries 20 ml of oxygen. (*Assuming that a 100ml of blood contains about 15g of hemoglobin).*
    - Plasma also binds to and carries oxygen, but in very little amounts, similar to that of water. Therefore, a 100ml of plasma (only) carries 0.3 ml of oxygen. (The remaining 19.7ml of oxygen are carried by RBCs)

- ***Hemoglobin-Oxygen dissociation curve of an adult human:***
  - **The figure below shows the extent to which hemoglobin picks up and releases oxygen <u>as the oxygen pressure in the blood changes</u>.**
  - When blood passes through the **lungs**, where the partial pressure of oxygen is about **100 mm Hg**, the hemoglobin becomes about **97%** (not 100%) saturated with oxygen. (1)
  - When blood passes through **distant tissues**, where the partial pressure of oxygen is about **40 mm Hg**, hemoglobin releases almost **25%** of its oxygen (**75%** remains bound). (2)
  - When blood passes through **very distant tissues**, where the partial pressure of oxygen is about **25 mm Hg** (P_{50}), hemoglobin releases **50%** of its oxygen (half the oxygen content is bound and the other half is released). (3)



- **Oxygen content in the blood at different PO_2 (oxygen partial pressure) values and different hemoglobin concentrations:**
    - The figure below clearly shows that the amount of oxygen carried in a volume of blood is dependent on PO_2 as well as hemoglobin concentrations.
        - ✓ **The higher the PO_2, the higher the content of oxygen in the blood.**
        - ✓ **The higher the hemoglobin concentration, the higher the content of oxygen in blood.**



- On the other hand, the **percentage saturation of hemoglobin** with oxygen **is dependent on PO_2** and totally **independent of hemoglobin concentration**, as presented in the first figure.

- Thus, if oxygen content was plotted against PO_2, the level of the curve will be dependent on hemoglobin concentration of the sample of blood, and so, the curve will not be the same for all people as it depends on the hemoglobin concentration variations. (second figure)

- But when the percentage saturation of hemoglobin is plotted against PO_2, the level of the curve will always be the same, whatever the hemoglobin concentration is. Therefore, the plot will always be the same for all people, males and females. (first figure)

Conclusion:

- **Oxygen content in blood:**
  - ✓ Is dependent on PO_2 and hemoglobin concentration.
  - ✓ The plot of hemoglobin content against PO_2 is not identical in all blood samples depending on hemoglobin content.
- **Percentage saturation of hemoglobin:**
  - ✓ Is dependent on PO_2, but independent of hemoglobin concentration.
  - ✓ The plot is identical in all blood samples, regardless of hemoglobin content.

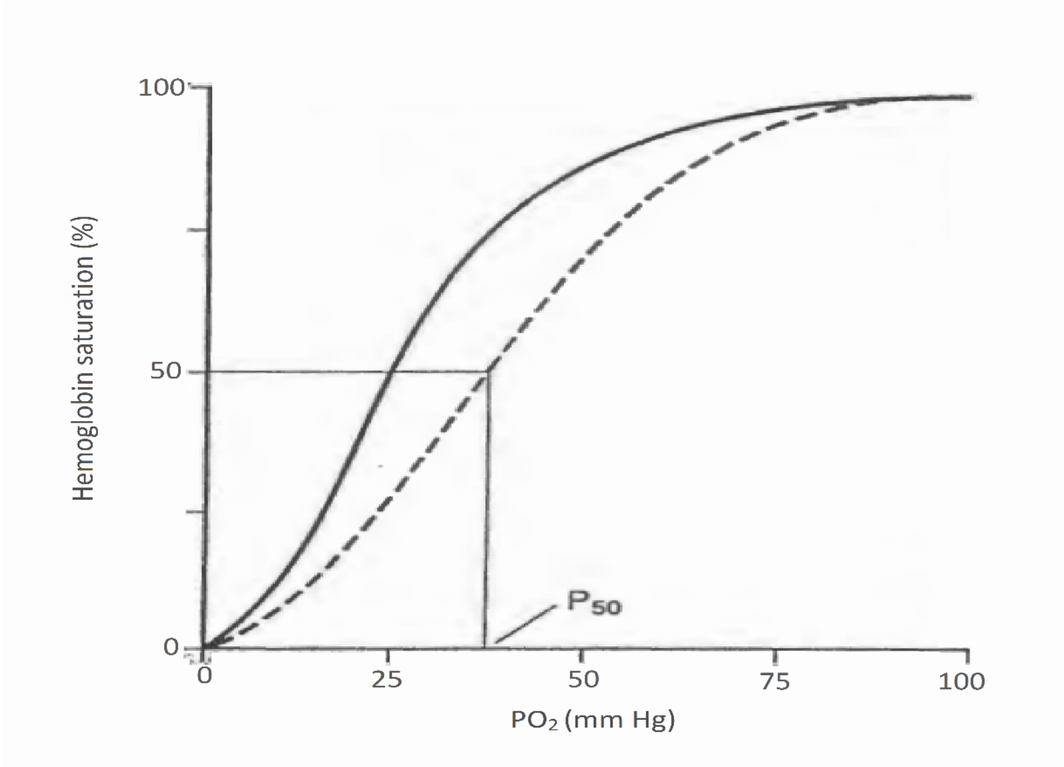
Note: The previous part was not mentioned this way during the lecture, I tried to clarify things as not to lead to any kind of confusion.

- As you know, hemoglobin contains 4 heme molecules that bind oxygen. These 4 heme molecules, however, do not bind to oxygen all at the same time. If the four heme molecules of ALL hemoglobin molecules of ALL RBCs bind oxygen at the same time, the person will collapse as no oxygen will remain in the lungs.
  Consequently, the binding of oxygen molecules occurs one by one. The binding of the first oxygen molecule facilitates the binding of the second, the binding of the second facilitates the binding of the third and so on.

- There are millions of hemoglobin molecules in a single RBC (at least 400 to 500 million).

Till now, we've seen the percentage saturation hemoglobin curve under physiological conditions. Now, we're going to discuss the changes that occur in the graph (shifting to the right or left) under **pathological or abnormal conditions**.

Shifting to the right:



Read the following very carefully (was not mentioned in the lecture):

- A rightward shift in the curve indicates that hemoglobin under study has a **decreased affinity for oxygen**.
- Decreased affinity of hemoglobin for oxygen makes it more difficult for hemoglobin to bind to oxygen (requiring higher partial oxygen pressure to achieve the same oxygen saturation). Thus, P_{50} (the partial pressure at which 50% of hemoglobin is saturated with oxygen) when there's a shift to the right is **higher than normal**.
- This decreased affinity, however, makes it **easier for hemoglobin to release the oxygen bound to it.**

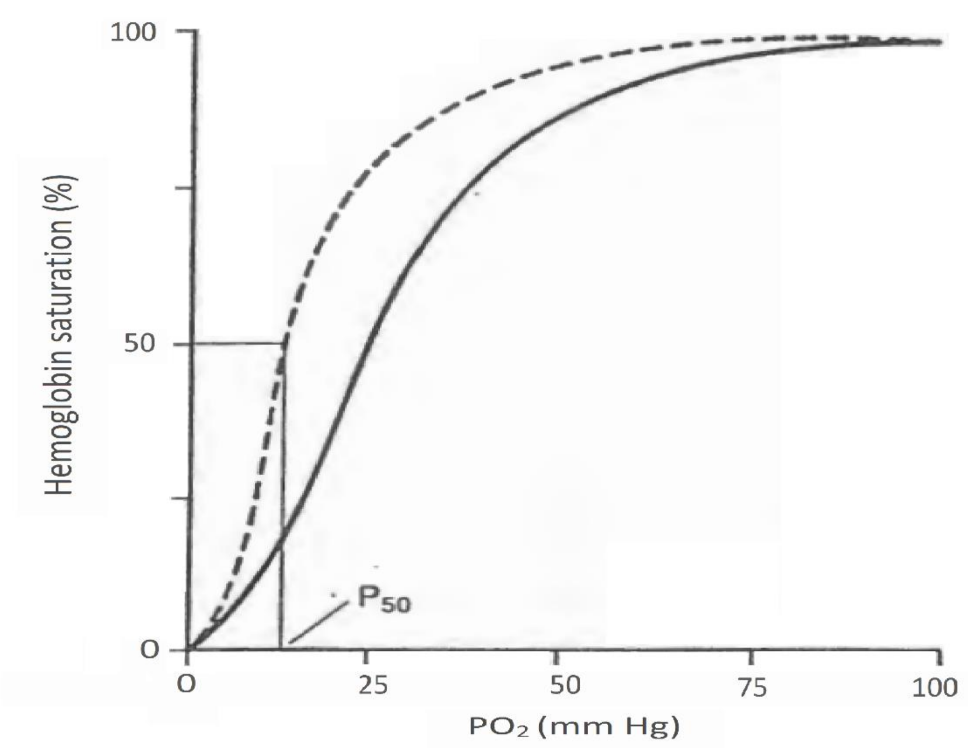
So, in right shifts:

- The affinity for binding oxygen decreases.
- P_{50} increases (here, it is slightly more than 30 mm Hg instead of 26 mm Hg) because the binding of hemoglobin to oxygen is more difficult.
- Oxygen release increases (due to decreased affinity for oxygen).
- This means that the body needs more oxygen (as during exercise or hemorrhagic loss ...Etc.)

Factors causing shifting to the right:

- ✓ High partial pressure of CO_2
- ✓ Low pH (high acidity)
- ✓ High temperature
- ✓ High concentration of 2,3-BPG (physiologic or pathologic)

Shifting to the left:



Read the following very carefully (was not mentioned during the lecture):

- Leftward shifts in the curve indicate that hemoglobin under study has an increased affinity for oxygen.
- This increased affinity makes it easier for hemoglobin to bind to oxygen (requiring lower partial oxygen pressure to achieve the same oxygen saturation). Thus, P_{50} (the partial pressure of oxygen at which 50% of hemoglobin is saturated with oxygen) is lower than normal.
- This increased affinity, however, makes it more difficult for hemoglobin to release the oxygen bound to it. And so, oxygen release decreases.

So, in left shifts:

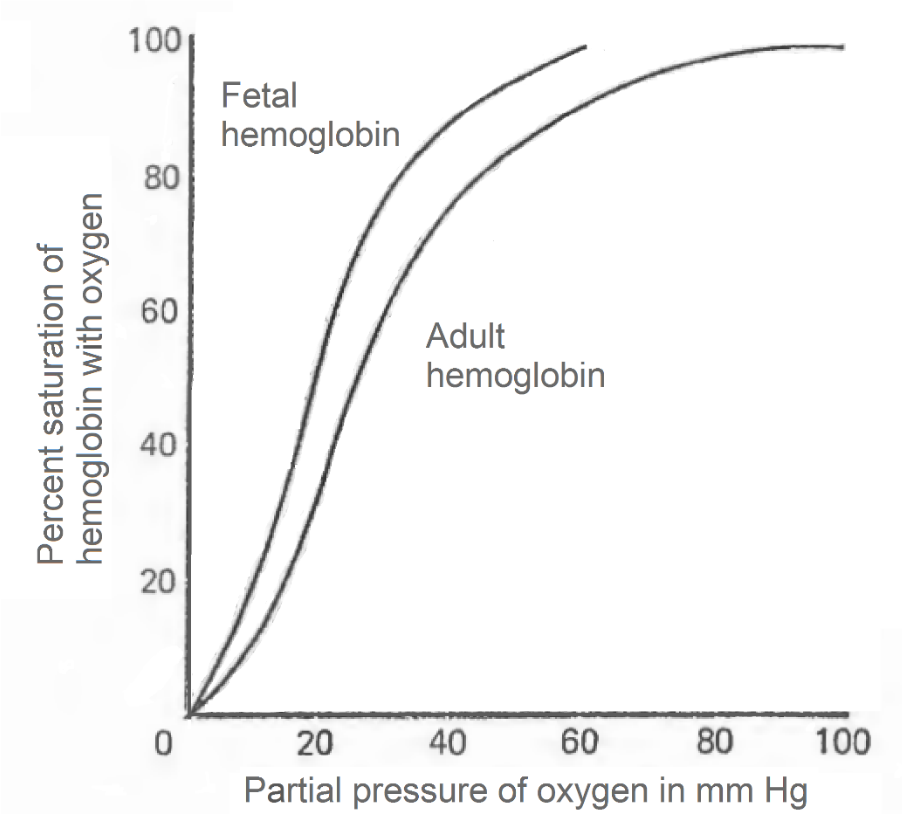
- The affinity of hemoglobin to oxygen increases.
- P_{50} decreases (here it is less than 20 mm Hg instead of 26 mm Hg)
- Oxygen release decreases (in physiological or pathological conditions)

Factors causing shifting to the left:

- ✓ Low partial pressure of CO2
- ✓ High pH (low acidity)
- ✓ Low temperature
- ✓ Low concentration of 2,3-BPG

- **Physiological conditions vs. pathological conditions:**

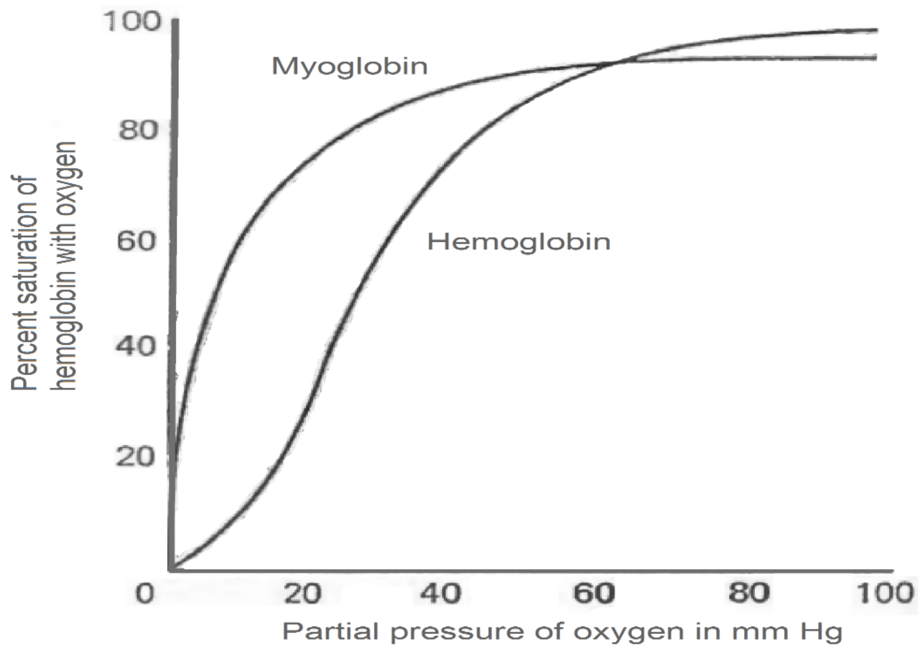
Physiological conditions→ fetal hemoglobin in the **fetus.**
Pathological conditions→ high concentration of fetal hemoglobin in **adults.**



- As presented in the figure, the fetal hemoglobin curve is on the left of the one for maternal hemoglobin indicating that fetal hemoglobin has a higher affinity for oxygen. Hence, when the mother's blood enters the placenta, it transfers oxygen to the blood of the fetus.

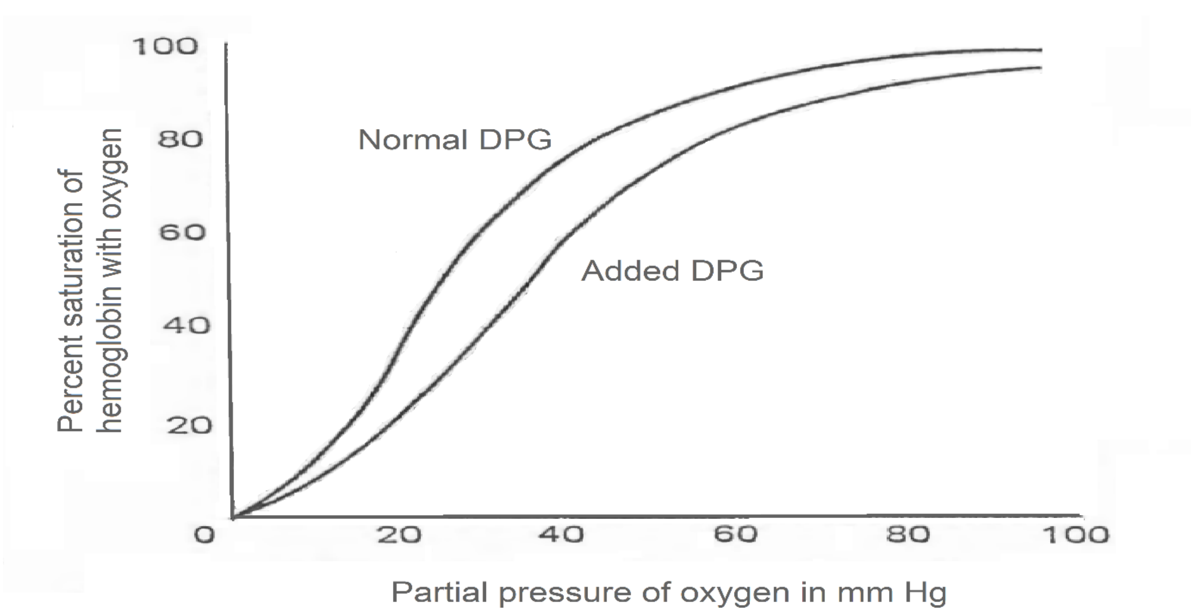
Hemoglobin vs. Myoglobin:

- **Myoglobin curve is shifted to the left, and this makes sense as myoglobin doesn't release oxygen unless PO_2 is very low.**



- As you can see, the dissociation curve of myoglobin (muscle hemoglobin) is far to the left of that for adult hemoglobin and has a hyperbolic shape. Thus, hemoglobin transfers oxygen readily to myoglobin. Myoglobin stores this oxygen until the oxygen pressure drops as in exercise. Then the myoglobin releases oxygen to be used in cellular respiration.

The effects of 2,3-Bisphosphoglycerate on oxygen dissociation from hemoglobin:



- The formation of extra DPG by red blood cells, as occurs in high altitudes, shifts the dissociation curve to the right. In other words, DPG promotes the release of oxygen from hemoglobin. This makes sense as in high altitudes (hypoxia) we need higher oxygen supply.

  Note: DPG (2,3-BPG) is the most abundant organic phosphate in the RBC, where its concentration is approximately that of hemoglobin. 2,3-BPG is synthesized from an intermediate of the glycolytic pathway- Lippincott

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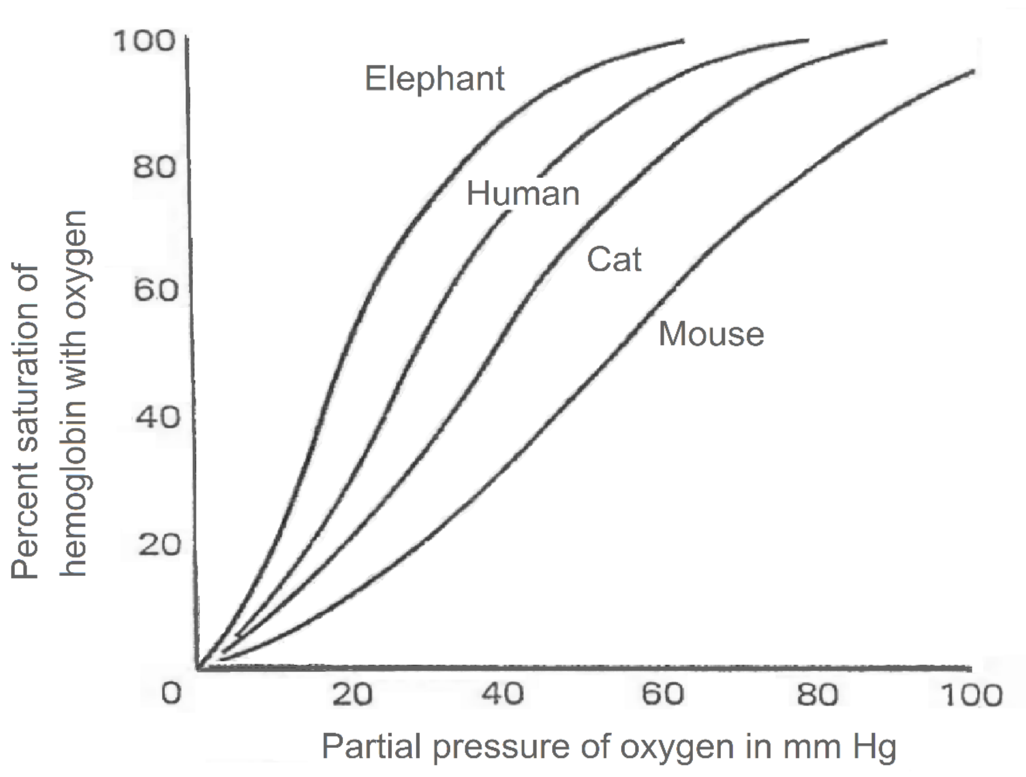
Effects of mammalian size on oxygen dissociation from hemoglobin:



- As you can see in the previous figure, small mammlas release oxygen more readily from hemoglobin than do large mammlas. This difference is probably due to the greater need of oxygen in small mammlas to support a greater heat production per unit of body weight.
  Note: Dr. Saleem thinks that it is based on **activity** (elephants are lazy, for example).

Blood parameters (erythrocyte):

- By now, you know some of these blood parameters including RBC count, hematocrit (45%), hemoglobin concentration (~15g/100ml).
  However, there are other blood parameters you should be familiar with, including their calculations:

  Note:
  - RCC: Red blood Cell Count
  - HCT: Hematocrit
  - MCH: Mean Corpuscular (RBC) Hemoglobin
  - MCHC: Mean Corpuscular Hemoglobin Concentration
  - MCV: Mean Cell Volume
  - pg: picogram (1 g = 10^{12} pg)

- **MCH = [Hb]/RCC**
  - The mean corpuscular hemoglobin indicates the average (mean) weight of hemoglobin in the red blood cell, but without taking the volume of the RBC into consideration.
  - Normal value for the MCH = 27-30 pg.
  - An MCH lower than 27 pg is found in microcytic anemia, and also in hypochromic, normocytic red blood cells.
  - Elevation of MCH occurs in macrocytic anemias and in some cases of spherocytocis in which hyperchromia occurs.

- **MCHC= [Hb]/HCT**
  - The mean corpuscular hemoglobin concentration is an expression of the average concenration of hemoglobin in the rod blood cells. It gives the ratio of the weight of hemoglobin to the volume of the red blood cell. (we relate hemoglobin weight to MCV).
  - Normal value of MCHC = 32-36% of MCV.
  - An MCHC below 32% indicates hpochromia.
  - An MCHC above 36% indicates hyperchromia.
  - Red blood cells with normal MCHC are termed normochromic.

- **MCV= HCT/RCC**
  - The normal value of MCV is around 80-90 μm^3 (or femtoliter).
  - Below 80: microcytic anemia (causes might be iron deficincy anemia, sediroblastic anemia and thalassemia).
  - Above ~97: macrocytic anemia (vitamin B12 deficiency and folic acid deficiency anemia).

    - **We look for MCH and MCHC to determine whether it is hypochromia, hyperchromia or normochromia.**
    - **We look for MCV to determine whether it is microcytosis, macrocytosis or normocytosis.**

The End

روحٌ حزينة بإمكانها أن تقتل الإنسان أسرع من جرثومة.. لا تحزن.

This sheet has been corrected and edited.