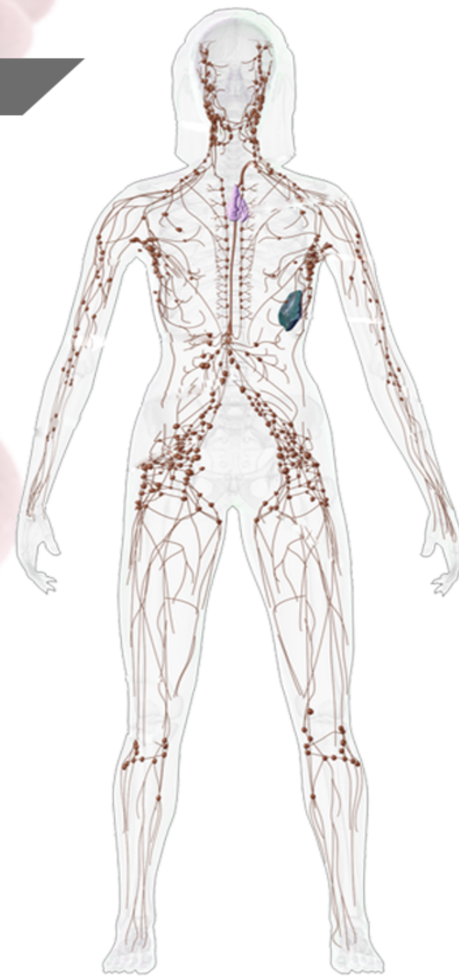
Sheet 4

Hematology and Lymphatic system

Subject | Physiology



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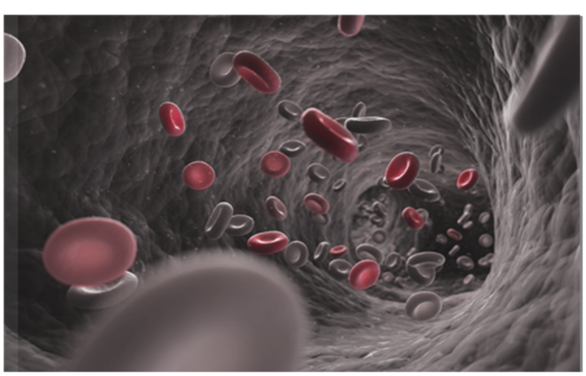


*The doctor started the lecture with the structure of hemoglobin stating that it has **four** hemes and each one of them carries an oxygen molecule.*

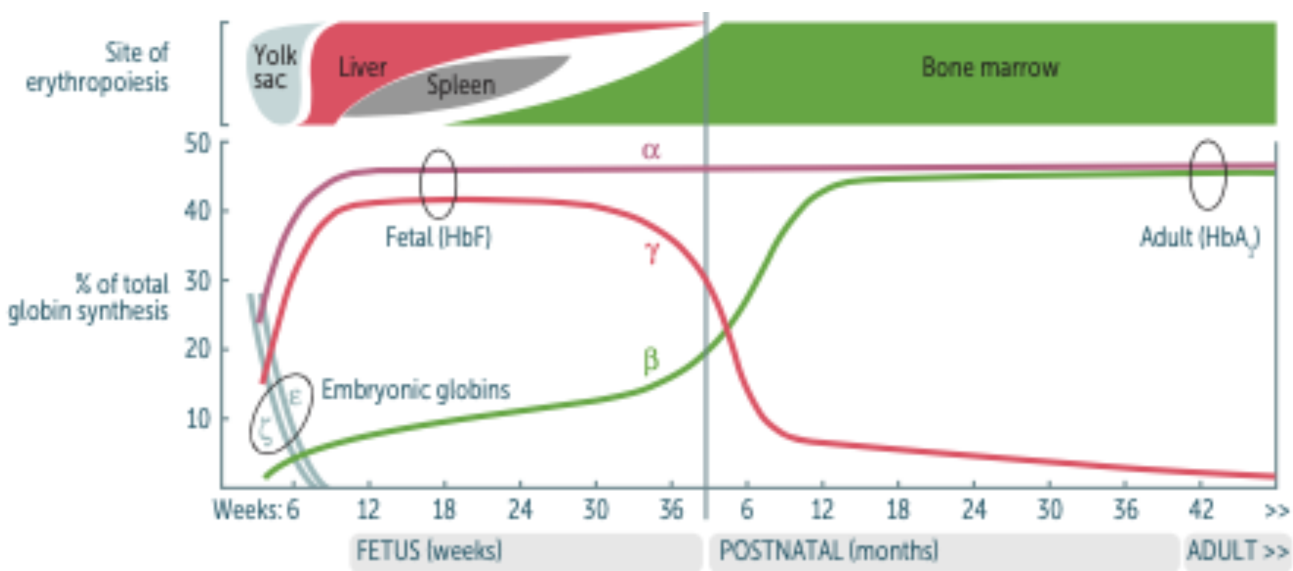
* There are 250.000.000 hemoglobin molecules in one RBC

Name	Designation	Molecular Structure	Proportion in Adults	Proportion in Newborns
Adult hemoglobin	A	$\alpha_2\beta_2$	97%	20%
Hemoglobin A_2 **after birth**	A_2	$\alpha_2\delta_2$	2.5%	0.5%
Fetal hemoglobin	F	$\alpha_2\gamma_2$	<1%	80%
Portland		$\zeta_2\gamma_2$	0	0
Gower I **embryo**		$\zeta_2\epsilon_2$	0	0
Gower II		$\alpha_2\epsilon_2$	0	0

in total we have 8 oxygen-carrying molecules; 6 hemoglobins, myoglobin (in muscles) and neuroglobin (in brain)

* **Fetal hemoglobin gradually decreases after birth until totally replaced by the 6th month.**

* **Fetal hemoglobin is present in all RBCs.**



Alpha Always, Gamma Goes Becomes Beta

Oxygen-hemoglobin dissociation curve

from this curve we notice the following:

1-**when PO2 is 100 mm Hg in the lungs,** the hemoglobin does not become 100% saturated, **only 97%** of it will be saturated.

2- At tissue level when PO2 is **40 mmHg** not the whole oxygen is released just **25% is released,** 75% remains bound to hemoglobin.

3-The value of PO2, when **50%** of hemoglobin is saturated, is **26mm Hg**.

The previous curve is the normal curve that we find in all normal people **despite their hemoglobin concentration**, it represents the dissociation of hemoglobin, the release of oxygen at tissue level, and the P50, please note that it has nothing to do with hemoglobin concentration.

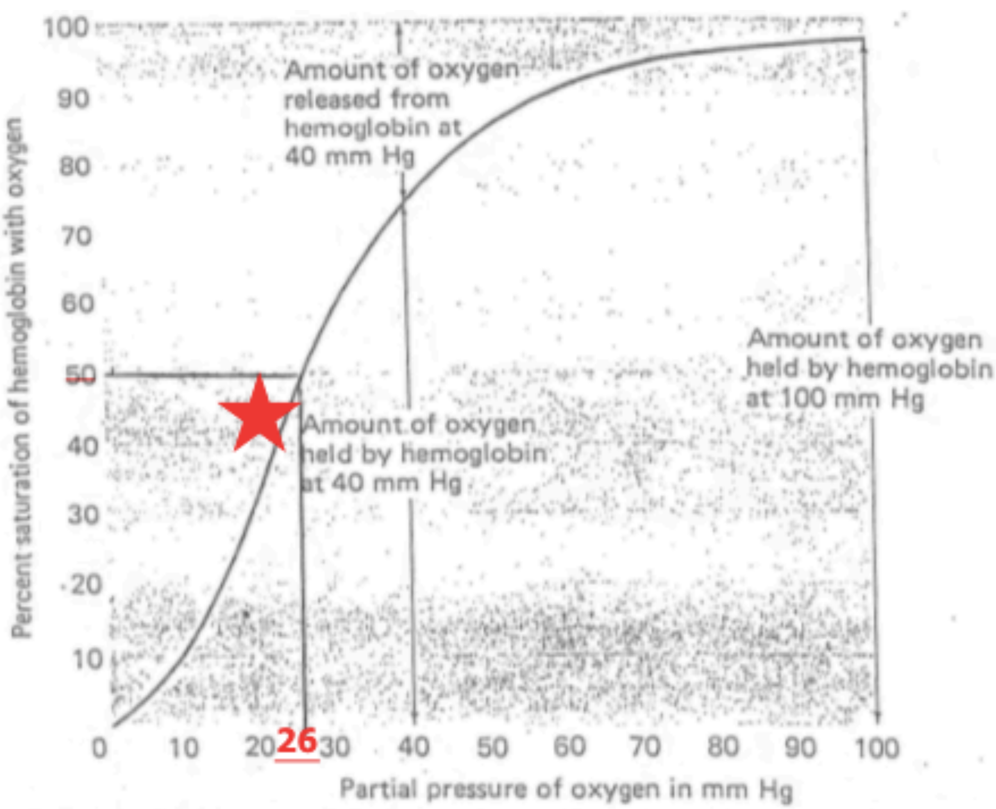
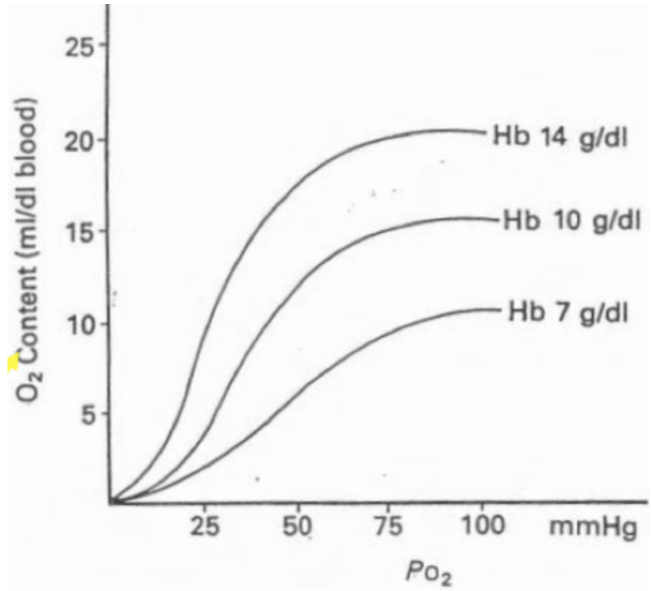


Figure 17.15 Hemoglobin Dissociation Curve for Oxygen in an Adult Human. The curve shows the extent to which hemoglobin picks up or releases oxygen as the oxygen pressure in the blood changes. 1 When blood passes through the lungs, where the partial pressure of oxygen is about 100 mm Hg, the hemoglobin becomes about 97 percent saturated with oxygen. 2 But when blood passes through distant tissues, where the partial pressure of oxygen is ordinarily about 40 mm Hg, the hemoglobin releases about 25 percent of its oxygen. (Adapted from J. W. Severinghaus, *J. Appl. Physiol.* 21 [1966]:1111:)

When we plot oxygen content against PO2 depending on the **hemoglobin concentration, we get **__different__ curves**. As shown in the figure.



This figure shows the oxygen content in the blood at different hemoglobin concentration: at 7g/dl,10g/dl and 14g/dl.

Quick scenario:

Imagine that spongebob is a red blood cell, a hemoglobin molecule is a net and the jellyfish are oxygen molecules

The amount of jellyfish sponge bob catches depend on 2 things; the concentration of jellyfish and the number of nets. If the concentration of jellyfish is high he is more likely to catch one, so as the number of nets, a high number of those makes it more likely a jellyfish would bump into one.

Sooo the oxygen content depends on:

1- **The partial pressure of oxygen** (PO2), The higher the PO2, the higher the content of oxygen in the blood.

2-**The concentration of hemoglobin**. The higher the hemoglobin concentration, the higher the content of oxygen in blood.

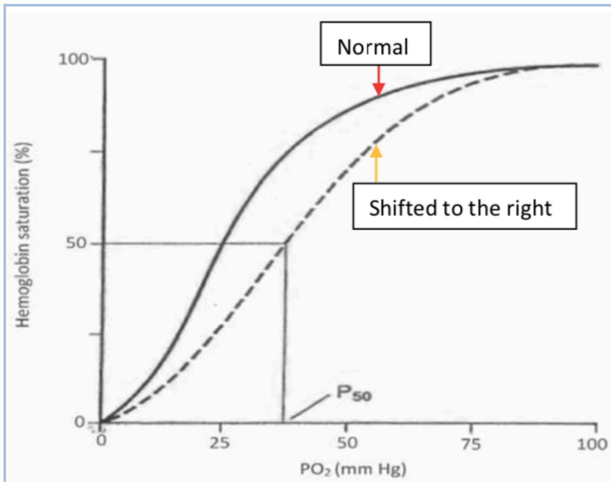
*** The percentage of hemoglobin saturation with oxygen is **dependent on PO2** and it is **INDEPENDENT of hemoglobin concentration**.

— So, if oxygen content is plotted against PO2, 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 PO2, the level of the curve will always be the same, whatever the hemoglobin concentration is (***independent***). Therefore, the plot will always be the same for all people, males and females.(first figure)

***** Remember that hemoglobin, consists of 4 subunits, each one is bound to a heme. so it is a total of 4 heme groups for the whole hemoglobin molecule. Each heme group binds to 1 oxygen molecule, so overall the whole hemoglobin binds to 4 oxygen molecules. However, these hemes do not bind oxygen all at the same time. Consequently, the binding of oxygen molecules occurs one by one (cooperativity).*

$$Hb_4 + O_2 \rightleftarrows Hb_4O_2$$
$$Hb_4O_2 + O_2 \rightleftarrows Hb_4O_4$$
$$Hb_4O_4 + O_2 \rightleftarrows Hb_4O_6$$
$$Hb_4O_6 + O_2 \rightleftarrows Hb_4O_8$$

Combination of the first heme in the Hb molecule with O_2 increases the affinity of the second heme for O_2, and oxygenation of the second increases the affinity of the third, etc, so that the affinity of Hb for the fourth O_2 molecule is many times that for the first. ****



We have to 2 curves one is normal and one is shifted to the ***right*** *.How to know whether it's normal or shifted?*

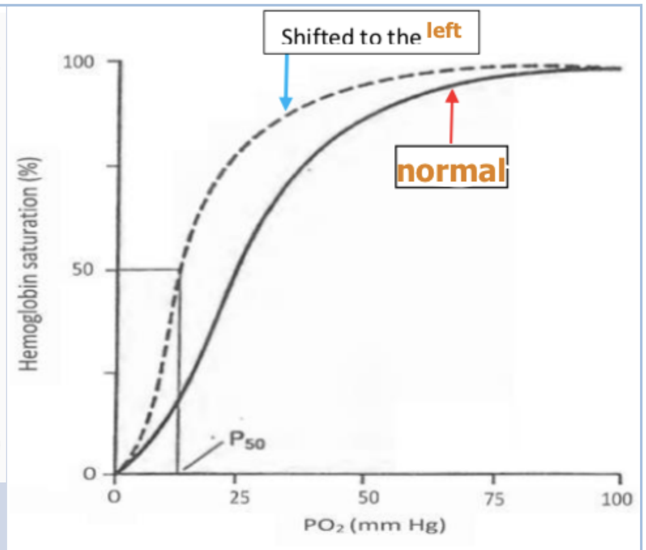
by the value of p50 which is 26 mm Hg, so the normal curve must have the value of PO2 equal to 26 mm Hg when the hemoglobin saturation is 50%.

<u>**Causes**</u>:

1) increase partial pressure of CO_2.
2) decrease pH (high acidity)
3) increase temperature
4) increase the concentration of 2,3-BPG (physiologic or pathologic)

<u>**Results:**</u>

1) The affinity of hemoglobin toward oxygen decreases, and this means that the body needs more oxygen.
2) P50 increases (here, it is slightly more than 30 mm Hg)
3) Decreased affinity for oxygen —> ***increase oxygen release from hemoglobin.***



We have to 2 curves one is normal and one is shifted to the ***left*** *.How did we know it's shifted to the left?*

Same thing, ***by the value of p50,*** the normal curve has a p50 value of 26 whereas the curve shifted to the left has a value of less than that.

<u>**Causes**</u>:

1) decrease partial pressure of CO_2.
2) increase pH (low acidity).
3) decrease temperature.
4) decrease concentration of 2,3-BPG.

<u>**Results:**</u>

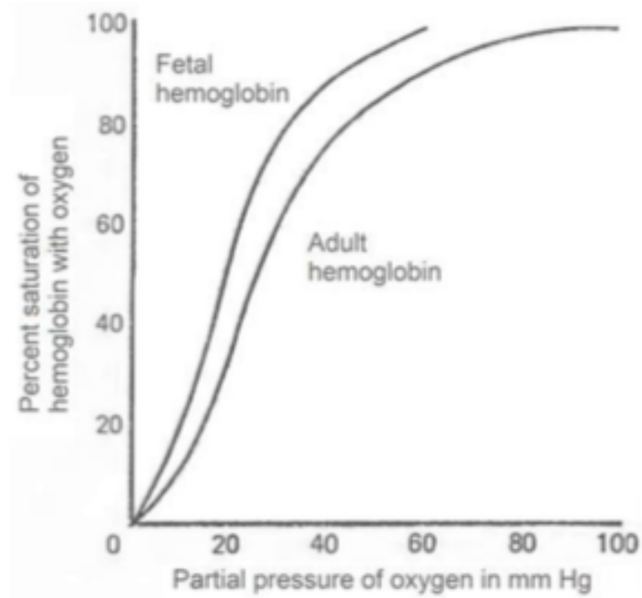
1) The affinity of hemoglobin toward oxygen increases.(the body doesn't need too much oxygen)
2) P50 decreases
3) Increased affinity for oxygen —> ***decreased oxygen release from hemoglobin.***

Q: what the different between oxygenation and oxidation?

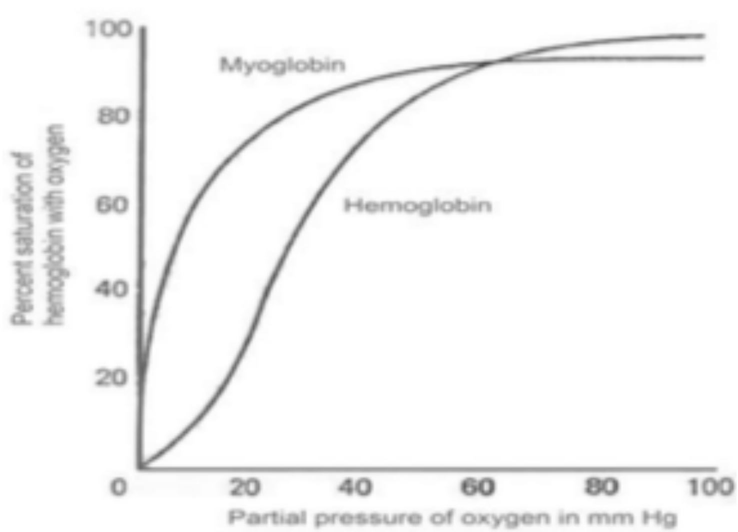
***Oxidation**: binding of oxygen and not releasing it "irreversible".*

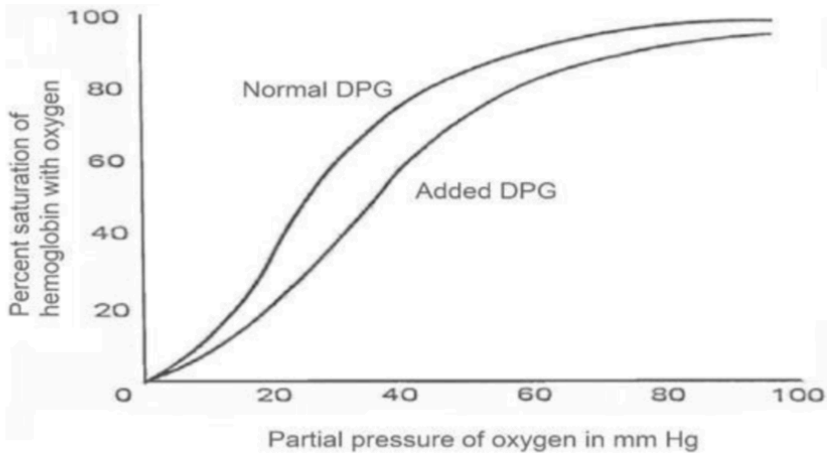
***Oxygenation**: binding of oxygen and releasing it "reversible"*

- There are two types of hemoglobin presented in this figure the fetal hemoglobin and the adult hemoglobin. **The fetal hemoglobin has higher affinity for oxygen**. So, fetal hemoglobin doesn't release oxygen easily **unless the pO2 is low**. *The importance of this difference in the affinity comes when the mother's blood enters the placenta, it transfers oxygen to the blood of the fetus.* (because fetal Hb has higher affinity toward oxygen than adult Hb).



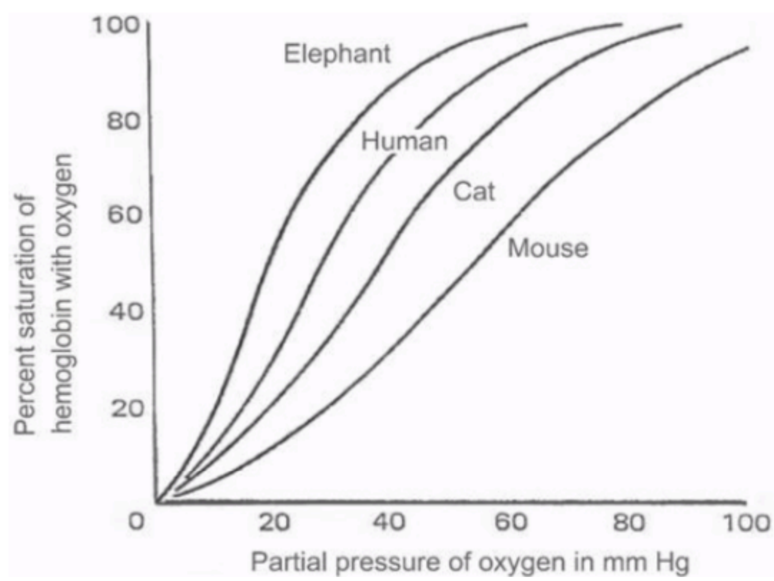
- As you can see, the dissociation curve of myoglobin is far to the left of that for adult hemoglobin and has a **hyperbolic shape**. *Thus, hemoglobin transfers oxygen to myoglobin as myoglobin has higher affinity toward oxygen than hemoglobin* (even higher than fetal hemoglobin). Myoglobin stores this oxygen until the oxygen pressure drops(ex: exercise). Then myoglobin releases oxygen to be used in cellular respiration.
- Myoglobin in muscle doesn't release oxygen easily unless pO2 is very low.





- 2,3-DPG **normally increases** due to **hypoxia** and it reduces the affinity of hemoglobin toward oxygen. The formation of extra DPG by red blood cells, as occurs in high altitudes, shifts the dissociation curve to the right. This means that in such areas oxygen is released more easily, and this makes sense as in high altitudes (hypoxia) we need higher oxygen supply.

This figure represents the oxygen dissociation curve of different kind of mammalians and you can notice the following: The elephant curve is shifted to the left (compared to human curve) meaning it's Hb has higher affinity (lower oxygen need). As for the cat and the mouse curves they are shifted to the right (compared to human curve) meaning that their Hb has lower affinity (higher oxygen need). The reason of this difference in affinity is that the demand of oxygen in each mammalian differs according to its activity.



Blood parameters (erythrocytes) *by now you know:*

- **RBC** or ERCS (RBC count). men: 4.7 to 5.5 mcL, women: 4.2 to 5 mcL. { mcL: Million cell per liter}
- **HCT** (hematocrit). men: 45% of blood, females: 40%
- **Hemoglobin concentration**: in males: 16g, in females: 14g (~15g/100ml).
- MCV (Mean Corpuscular Volume): 80-90 micron cubic or pg. {pg= pictogram (1 g = 10^12 pg)}.

Other parameters:

Mean Corpuscular Hemoglobin (MCH)

The MCH indicates the average weight of hemoglobin in the red blood cell.

$$MCH = \frac{\text{Weight of hemoglobin in 1 } \mu l \text{ of blood}}{\text{Number of red blood cells in 1 } \mu l \text{ of blood}}$$

$$MCH = \frac{\text{Hemoglobin} \times 10}{\text{Red blood cell count in millions}} \text{ pg}$$

Normal value for the MCH: 27–31 pg

The MCH indicates the amount of hemoglobin in the red blood cell and **should always correlate with the MCV and MCHC**. An MCH **lower than 27 pg** is found in *microcytic anemia* and also with *normocytic*, *hypochromic* red blood cells. An **elevated MCH** occurs in *macrocytic anemias* and in some cases of *spherocytosis* in which *hyperchromia* may be present.

Mean Corpuscular hemoglobin Concentration (MCHC)

The MCHC is an expression of the average concentration of hemoglobin in tho red blood cells. It gives the ratio of the weight of hemoglobin to the volume of the red blood cell.

$$\text{MCHC} = \frac{\text{Hemoglobin in g/dl}}{\text{Hematocrit/dl}} \times 100 \text{ (to convert to \%)}$$

$$\text{MCHC} = \frac{\text{Hemoglobin} \times 100}{\text{Hematocrit}} \%$$

Normal value for the MCHC: 32–36%

The MCHC indicates whether the red blood cells are normochrormic, hypochromic, or hyperchromic. An MCHC below 32% indicates *hypochromia*, an MCHC above 36% indicates *hyperchromia*, and red blood cells with a normal MCHC are termed *normochromic.*

Mean corpuscular volume (MCV)

The mcv indicates the average volume of the RBCs.

$$\text{MCV} = \frac{\text{Volume of red blood cells in femtoliters (fl)}/\mu\text{l of blood}}{\text{Red blood cells}/\mu\text{l of blood}}$$

$$\text{MCV} = \frac{\text{Hematocrit} \times 10}{\text{Red blood cell count in millions}} \text{ fl}$$

Normal value for the MCV: 80–97 fl

The MCV indicates whether the red blood cells appear normocytic, microcytic or macrocytic. If the MCV is less than 80 fl, the red blood cells are *microcytic*. If the MCV is greater than 97 fl, the red blood cells are *macrocytic*. If the MCV is within the normal range, the red blood cells are *normocytic*.

THESE EXAMPLES ARE FROM LECTURE 5

Below you have parameter values measured from different blood samples, describe the RBCs in each one of them:

1.

MCV= 67

MCH= 22 *microcytic/ normormochromic*

MCHC= 33

2.

MCV= 91

MCH= 31 *normocytic/ normochromic*

MCHC= 39

3.

MCV= 69

MCH= 20 *microcytic/ hypochromic*

MCHC= 30

4.

MCV= 113

MCH= 38 *macrocytic/ normochromic*

MCHC= 33