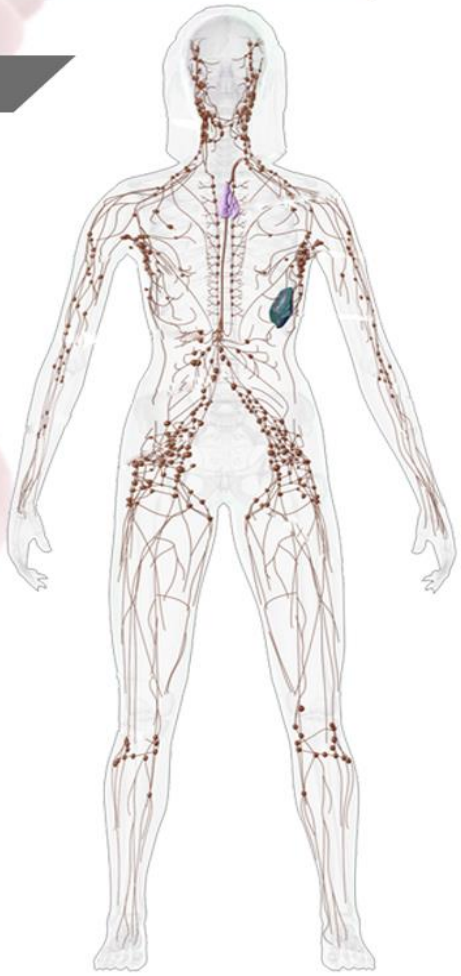
Sheet 1

Hematology and Lymphatic system

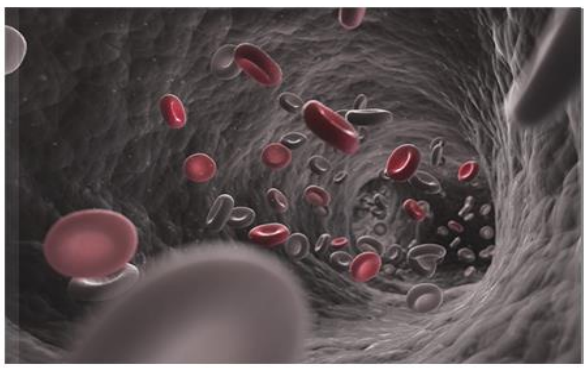
Subject | Pathology Online L1



Done by | Razan al-zoubi

Corrected by | Bann Khraisat

Doctor | Ahmad T. Mansour



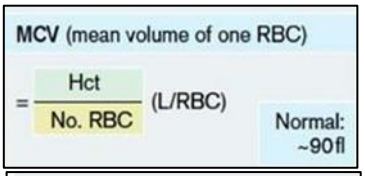
Introduction to **ANEMIA**:

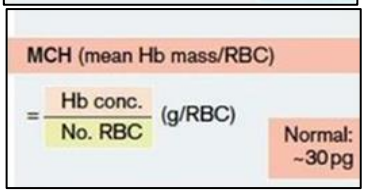
What is Anemia?!

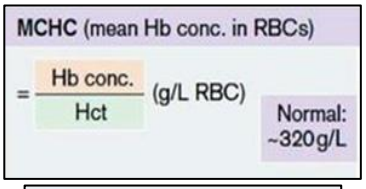
Anemia is…

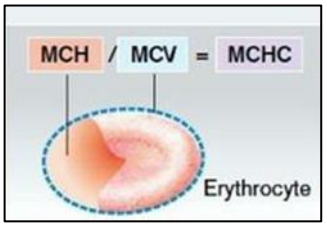
- *The reduction in the **oxygen-transporting capacity** of blood, which usually results from a **decrease in the red cell mass** to subnormal levels.*
- This decrease is reflected in **the decrease in hematocrit** or **hemoglobin concentration.** (majority of the time but not always… check page 3)

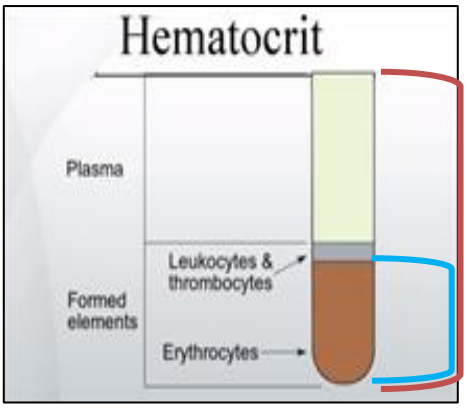
- **Some RBCs parameters:**
  1- **Mean cell volume (MCV):** the average volume of a red cell expressed in femtoliters (*fL*). (very important for classification of anemia).
  2- **Mean cell hemoglobin (MCH):** the average content (mass) of hemoglobin per red cell, expressed in *pictograms*.
  3- **Mean cell hemoglobin concentration (MCHC):** the average concentration of hemoglobin in a given volume of packed red cells, expressed in *grams per deciliter*.
  4- **Red cell distribution width (RDW):** the coefficient of variation of red cell volume (this number explains how variable the sizes of RBCs in a sample are). Thus, it is important in differentiating between iron deficiency anemia and thalassemia, since both show microcytic anemia (low MCV). However, RDW is **high in iron deficiency anemia**, and **low to normal in thalassemia.**
  5- **Hematocrit:** the ratio of packed red cells volume to total blood volume.
  ➔ How to calculate hematocrit?
  - Divide the length of the packed RBCs in the tube over the sum of plasma and RBCs length.
  6- **RBC count**: the number of RBCs per unit volume, *(usually expressed in millions) /microliter*, for example $5x10^6$/microliter.











An example of normal reference ranges of RBCs parameters:

Measurement (units)	Men	Women
Hemoglobin (gm/dL)	13.6-17.2	12.0-15.0
Hematocrit (%)	39-49	33-43
Red cell count ($\times 10^6/\mu L$)	4.3-5.9	3.5-5.0
Reticulocyte count (%)	0.5-1.5	
Mean cell volume (fL)	82-96	
Mean cell hemoglobin (pg)	27-33	
Mean cell hemoglobin concentration (gm/dL)	33-37	
Red cell distribution width	11.5-14.5	

- The doctor said not to memorize any numbers in this table, since each laboratory is required to establish its own reference ranges of RBCs parameters based on its population. So, it's important to look at the reference range that is suitable for each patient.

Question time!!!

1- 45-year-old male, was injured in a car accident, he bled profusely. Upon presentation he was obtunded (dull), pale and distressed (decreased mental capacity).

- Vital signs were as follows:

  heart rate 140 beat/minute----- increased

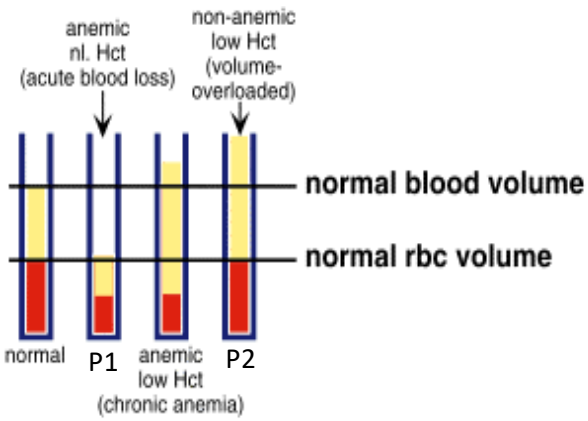
  Respiratory rate 25/minute---- increased

  Blood pressure 80/30---------- very low

- His hemoglobin and hematocrit were **within reference range.**

2- A 29-year-old female, 8months pregnant, in a routine prenatal visit, she did a CBC (complete blood count), and was found to have a **hematocrit that is slightly below normal limits**.

Now, which one of these patients is anemic?



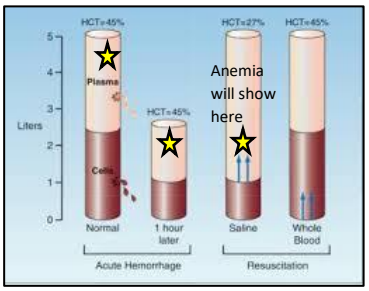
- **Patient (1) (the 2nd tube to the left)**

This patient is considered **ANEMIC**

Although the Hct (hematocrit) is within the normal range, because the patient has lost proportionate amounts of both plasma and RBCs, in reality this patient has lost blood (*acute blood loss*).

Remember: Anemia by definition is the loss of RBCs.

- At presentation, if CBC was done, then Hematocrit will be within the normal reference range, however if the patient is resuscitated and received intravascular fluid, the patient's plasma will expand while the RBCs mass will be the same, and hence anemia will show.
- This picture might help in understanding this:



- **Patient (2) (the tube on the right)**

This pregnant lady is **NOT ANEMIC**

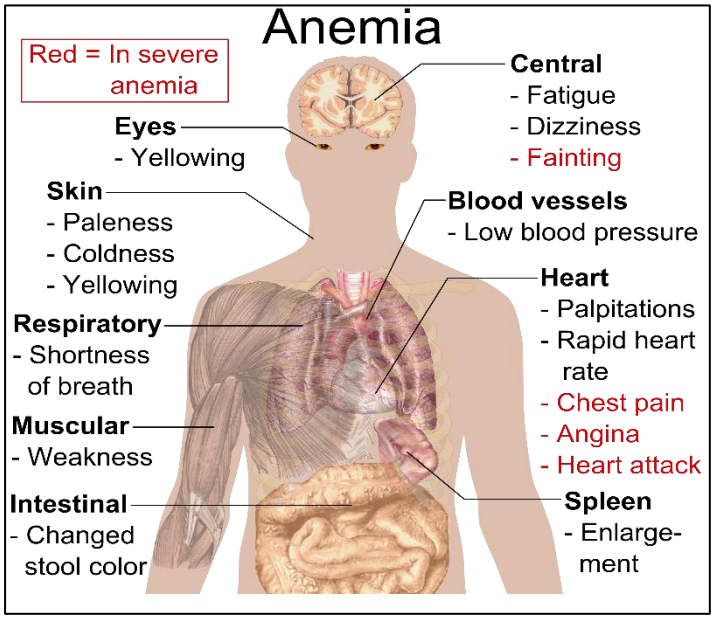
Hct is low, and that is because pregnant ladies will have retention of fluids (buildup of fluid ~ Swelling is a normal part of pregnancy that is caused by additional blood and fluid), HOWEVER there is no actual loss of RBCs mass.

Regarding the 3rd tube to the left, it presents a patient with **chronic anemia**, where there is a problem with the production of RBCs, or a problem in the maintenance and survival of RBCs, hence there is a loss of RBCs mass while the plasma is normal, **so hematocrit is low**.

Always remember: WE DO NOT TREAT NUMBERS WE TREAT PATIENTS!

Clinical manifestations of anemia: Result from decreased tissue oxygenation as well as from the underlying disease.

➔ ***However, anemia can be asymptomatic, and only caught when doing the CBC.***



The symptoms of anemia do not depend on its level, meaning that two patients who have the same level of hemoglobin, do not have to show the same symptomatology.

For example, if the patient is athletic, depending on his muscles ability, then a slight drop in the hemoglobin level might result in symptoms.

On the other hand, a patient who has a sedentary lifestyle, and is a couch potato might tolerate higher drops in Hb level.

In addition, the symptoms also depend on the underlying physiological condition of the patients themselves.

For example, an old man with underlying comorbidities will not be as tolerant to a drop in Hb as a young healthy patient.

What is the suggested **Work Up** for Anemia??

Depending on the **differential diagnosis**, a number of other blood tests also may be performed to evaluate anemia, including:

1) **Iron indices** (serum iron, serum iron-binding capacity, transferrin saturation, and serum ferritin concentrations), which help distinguish among anemias caused by **iron deficiency**, chronic disease, and thalassemia. (remember RDW is used in the differential diagnosis of thalassemia and iron deficiency anemia)

2) Plasma unconjugated **bilirubin**, **haptoglobin**, and **lactate dehydrogenase** levels, which are abnormal in **hemolytic anemias**.

3) Serum and red cell **folate** and **vitamin B12** concentrations, which are low in **megaloblastic (macrocytic) anemias.**

4) **Hemoglobin electrophoresis**, which is used to detect abnormal hemoglobin, used to detect hemoglobinopathies such as **thalassemia** and **sickle cell anemia**.

5) The **Coombs test**, which is used to detect **antibodies** coating RBCs and causing its hemolysis, in suspected cases of **immunohemolytic anemia.**

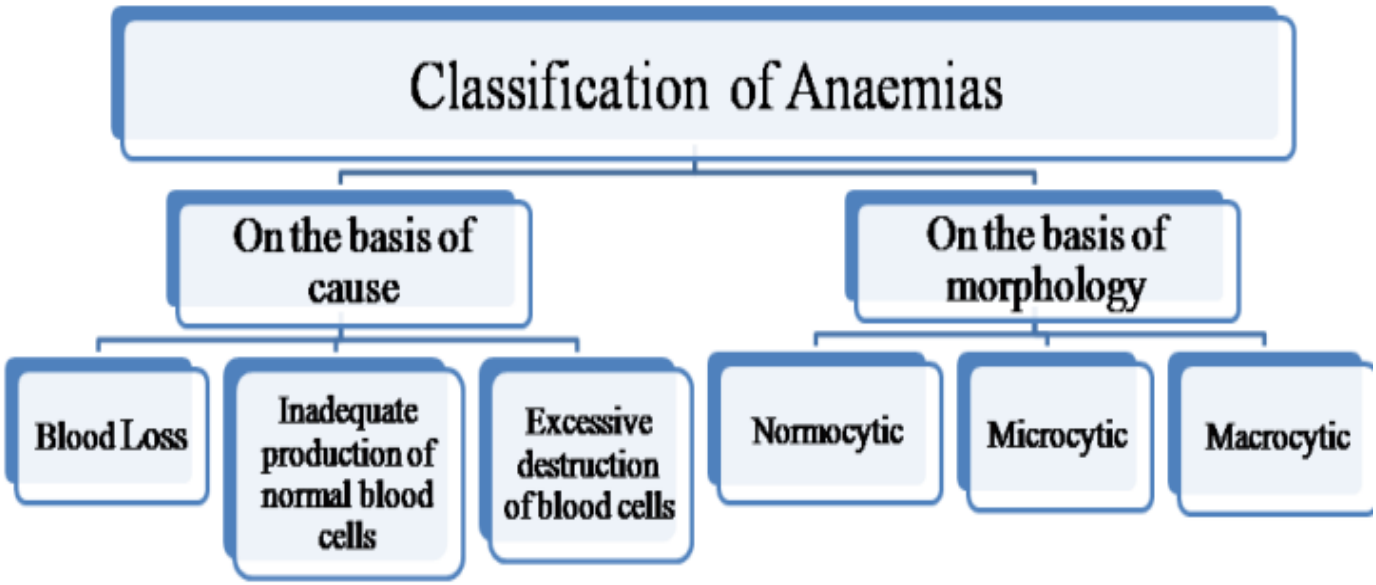
*We should always remember that we are **treating patients** not **numbers.***

So, in the case of **isolated anemia**, tests performed on the **peripheral blood** usually suffice to establish the cause.

For example, if you have an anemic young lady with no other cytopenias (normal platelet count, normal WBCs count) then examination of peripheral blood should be enough.

However, if the anemia is **associated with other cytopenias**, then a more serious etiology should be sought and a **bone marrow examination is warranted.**

For example, an elderly man with pancytopenia (anemia affecting RBCs, WBCs, and platelets), requires a more aggressive diagnosis such as bone marrow examination.



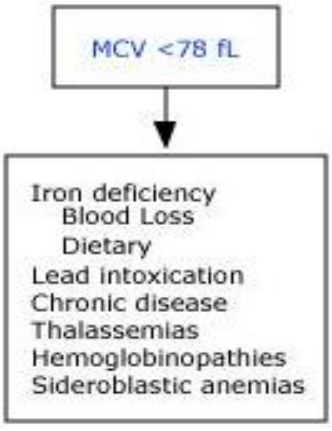
Classification of Anemias

On the basis of morphology (cell size):

- microcytic === low MCV
- macrocytic === high MCV
- normocytic === MCV within the reference range

*Causes of **microcytic anemia***:

♦ Iron deficiency anemia, and thalassemia are more common than lead poisoning and sideroblastic anemia (in which the blood has enough amounts of iron but cannot use it to make Hb).



*Causes of **macrocytic anemia**:*

- ♦ **Megaloblastic anemia**: mainly folate and vitamin B12 deficiency.
- ♦ **Non-megaloblastic anemia**: mainly hypothyroidism
- ♦ Liver disease and aplastic anemia.

- Micro and macrocytic anemias, are mainly **anemias of decreased bone marrow production.**

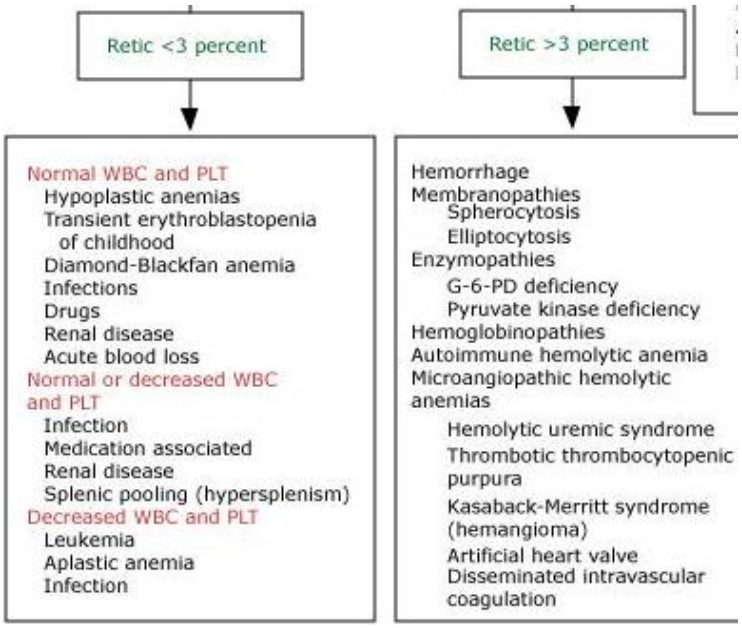
- This leaves the dichotomy of **decreased bone marrow production** versus **anemia of blood loss** to the **Normocytic anemias**.

Now how to differentiate between anemia of blood loss AND anemia of decreased bone marrow production??

- The answer is through **the reticulocyte count.**

- The reticulocyte is the precursor of the mature RBCs, it has no nucleus, but it has ribosomal remnants and that's why it looks darker than mature RBCs upon staining.

- The reticulocyte is produced in the bone marrow, then released into the blood and within 24-48 hours it becomes a mature RBC.



- So, if the anemia is caused by decreased bone marrow production, then **reticulocytes count will be low**.

- And if it is caused by blood loss at the peripheral level not at the bone marrow level (hemorrhage or hemolysis), the bone marrow will sense the anemia via the production of erythropoietin from the kidney, and RBCs production will increase trying to compensate, so **reticulocyte count will be high**.

Self Evalution Questions

1) Which one of the following parameters is used to assess the volume of the RBC?

   A. MCV
   B. MCHC
   C. RDW
   D. Hematocrit
   E. MCH

2) Which of the following is most helpful in the workup for immune hemolytic anemia?

   A. Iron indices
   B. Coombs test
   C. Hemoglobin electrophoresis
   D. Bone marrow examination

3) All of the following are examples of microcytic anemia, except:

   A. Iron deficiency anemia
   B. Thalassemia
   C. Megaloblastic anemia
   D. Lead poisoning
   E. Sideroblastic anemia

4) All the following are associated with increased reticulocyte count, except:

   A. Immune hemolytic anemia
   B. Spherocytosis
   C. Microangiopathic hemolytic anemia
   D. Aplastic anemia
   E. G6PD deficiency

5) All the following are clinical manifestations of anemia of diminished production, except:

   A. Skin pallor
   B. Shortness of breath
   C. Gallbladder stones
   D. Muscle weakness
   E. Confusion

A, B, C, D, C