Hematology

PATHOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number: 1

Subject: **Introduction to anemia**

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Introduction to anemia

Lecture 1 - Objectives covered in this sheet:

- **Definition of anemia**
- **Pathophysiology of anemia**
- **Classifications of anemia**

(You are required to study the sheets & Robbins Basic Pathology 9th ed., pages 408-425)

❖ Definition of anemia

In simple words: A reduction of oxygen delivery, secondary to decreased RBC mass.

- RBC mass as a lab test is difficult to do and time consuming, so, instead of it we measure hematocrit and haemoglobin concentration.

(Using hematocrit or hemoglobin concentration instead of RBC mass is **not** 100% accurate but it's more practical as we don't do RBC mass in daily basis.)

When we centrifuge blood using a test tube, packed RBCs will sink to the bottom of the tube, and plasma will stay at the top of the tube.

- Hematocrit = $\frac{\text{Length of packed RBCs in the tube } (L_{RBC})}{\text{The whole length of blood in the tube } (L_{blood})}$ expressed in %.
  - Low Hematocrit in most of the times indicate anemia.
- Hemoglobin concentration is calculated by a machine.
- Other parameter that can be used when we discus RBC disorders is RBC count; (expressed in number of cells per unit volume -mostly microliters /mm^3-)

  Blood cells can be counted using two ways:

  1) **The manual (old-fashion) way:** We place a volume of blood on a glass slide that has grooves on it presenting squares, each square will have a certain number of cells, we count the cells on squares and do some calculations to find average number of cells on the squares. This way is not being used anymore.

  2) **The new way:** A machine counts the number of cells. It is fast & accurate.

So hematocrit, hemoglobin concentration & RBC count are 3 parameters that we can measure. There are other 3 parameters that we can calculate, which are:

- Mean cell haemoglobin (**MCH**) ➔ $\frac{\text{Hemoglobin concentration}}{\text{Number of RBCs}}$
(Avg. amount of haemoglobin per 1 RBC)

- Mean cell volume (**MCV**) ➔ $\frac{\text{Hematocrit}}{\text{Number of RBCs}}$
(Average volume of RBCs)

- Mean cell haemoglobin concentration (**MCHC**) ➔ $\frac{\text{Hemoglobin concentration}}{\text{Hematocrit}}$
(Avg. volume haemoglobin in a given volume of RBCs)

- Red cell distribution width (**RDW**): It is the variation in the size of the RBCs. (It's important in the differential diagnosis of microcytic anemia);
RDW is high in **iron deficiency anemia**
RDW is normal in **thalassemia**

- MCV is important the classification of anemia; it can be used to distinguish between microcytic, macrocytic & normocytic anemia.
- There are reference ranges for these measured/calculated parameters in each city in the world. There are no universal reference ranges but the reference ranges are somehow close overall. (e.g. Hemoglobin in Jordan is different from haemoglobin in the US.) / (e.g.2. Hemoglobin in black Americans is different from haemoglobin in white Americans), etc…

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	

(This figure displays reference ranges in a particular city, the table is taken from Robbins. You **don't** have to memorize any of these numbers. Just have an idea)

Always whenever you do a CBC test (complete blood count) and look at a specific parameter, look at the reference ranges attached to it. (reference ranges of that company/hospital in that particular city).

Case 1

45 year old male, was injured in a car accident, he bled profusely, his symptoms were

- Obtunded (loss of consciousness)
- Pale skin
- Distress/Confusion
- High heart rate (140 beat/minute)
- High respiratory rate (25/minute)
- Low blood pressure (80/30)

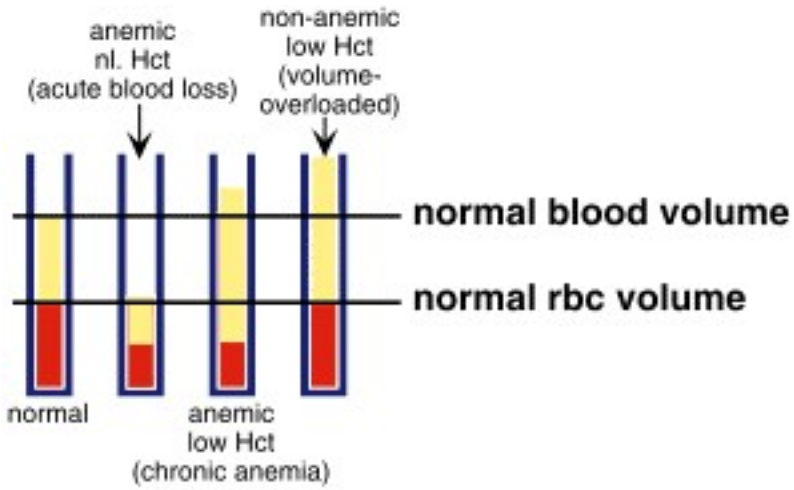
- His hemoglobin and hematocrit were **within reference range.**

Case 2

29 year old female, 8 months pregnant, in a routine prenatal visit, she was found to have a hematocrit that is slightly **below** normal limits

- ARE THESE 2 PATIENTS ANEMIC? We will find out.

Please look at the following figure:



When a patient loses high amount of blood and is taken to the emergency, the first thing the nurses do is give the patient normal Saline fluid to compensate the plasma he lost and then they do the CBC tests.

- RBCs and plasma are in almost equal proportions in blood (45% and 55%), so in **Case 1**, the patient lost plasma & RBCs in equal amounts, so Hemocrit will be normal although there **is** RBC loss, so the patient is ANEMIC. (Presented in tube 2)

  P.S.) The Hematocrit test here was done **before** giving the patient Saline!)

- In **Case 2**, the woman is pregnant and normally in pregnancy, there will be fluid retention in the body, so the plasma volume will increase and thus, Hematocrit decreases although there was **no** RBC loss. Here the patient is NOT ANEMIC. (Presented in tube 4)

- Apart from these 2 cases, Hematocrit is almost always related to RBC mass and anemia. (These 2 cases were exceptions)

- In the 3rd tube, both Hematocrit and RBC mass are low, thus it indicates anemia.

❖ Pathophysiology of anemia

In most of the times, anemia is chronic and asymptomatic.

Clinical manifestations of anemia are due to two factors:
-) The anemia itself (decreased O_2 delivery)
-) The underlying cause

✓ Symptoms due to the anemia itself are produced due to the fact that the body will try to compensate for that loss of oxygenation and that includes:
- Fast heart rate (tachycardia)
- High respiration rate/inhale of O_2
- Pale skin (blood will be shifted from skin to more vital organs)
- Muscle weakness

✓ Symptoms due to the underlying cause will be discussed in the next lectures, but for example, in "Iron deficiency anemia" patients will have:
- Nail abnormalities
- Esophageal webs
- Pica (happens in children; they will have appetite for inedible things)

In "Chronic hemolytic anemia" patients will have <u>gallbladder stones</u>.

- The severity of the symptoms can depend on the patient himself;
  - A person who is athletic will sense a small drop in haemoglobin
  - A person who is lazy will most likely NOT sense haemoglobin drop
- The severity of symptoms can depend on the underlying physiologic reserve;
  - e.g.) An old man with a weak heart function will not tolerate anemia as much as a young adult with good heart function that can compensate the O_2 loss better.

The differential diagnosis in case of suspecting anemia depends on the patient and on the underlying cause, so different tests other than a CBC is done depending on the patient's condition. For example, the differential diagnosis and the tests done for a young menstruating woman are different than the diagnosis of an old man with no symptoms, although both are anemic! So the work up differs from patient to another.

In case of suspecting the following anemias, you test for:

-) **Iron deficiency anemia →** Iron / Iron-binding capacity / ferritin / transferrin (Iron indices)

-) **Hemolytic anemia →** Plasma unconjugated bilirubin / haptoglobin / LDH

-) **Megaloblastic anemia →** Folate / Vitamin B12

-) **Thalassemia →** Hemoglobin electrophoresis

-) **Immunohemolytic anemia →** Coombs test

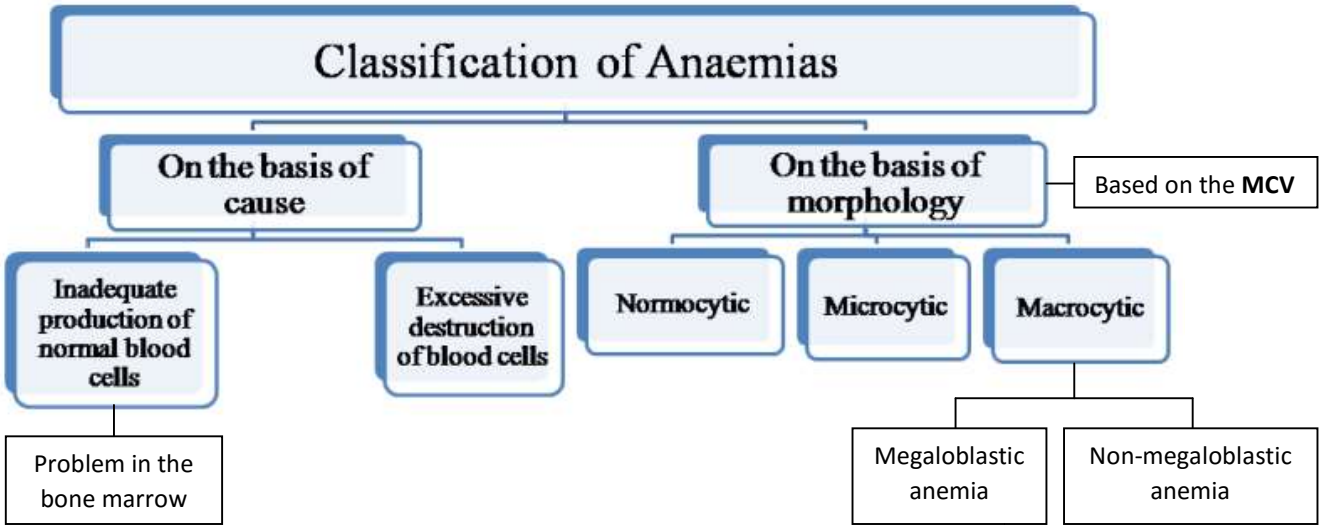
Immunohemolytic anemia is basically antibodies that fix on the surface of RBCs and attack them, Coombs test target these antibodies, if the test is positive then the patient has immunohemolytic anemia.

Isolated anemia: anemia with no decrease of other parameters in the blood (platelets & white blood cells).

The work up/differential diagnosis also depends on the findings that you can see on the CBC, for example:
For a young person with an isolated anemia, simple blood tests (e.g. Coombs & iron tests) will be enough. While for an elderly person with multiple cytopenias like blood with low platelets & WBCs, warmer and more invasive test that we save for more serious cases can be made (e.g. Bone marrow examination).

❖ Classification of anemia

It's importance lie in assisting in the **work up** & **treatment** that should be done.



- Microcytic anemia: MCV lower than the reference range.
- Macrocytic anemia: MCV higher than the reference range.
- Normocytic anemia: MCV is within the reference range.
  (They all have different differential diagnosis)

- The 4 major differential diagnosis for "Microcytic anemia" (All of the following lead to microcytic anemia):-
  - Iron deficiency
  - Thalassemia
  - Lead poisoning
  - Sideroblastic anemia

  (Sometimes Chronic diseases as well)

- The major differential diagnosis for "Macrocytic anemia":-

  -) **Megaloblastic**:

  - Vitamin B12 / Folate deficiency

  -) **Non-Megaloblastic**:

  - Alcohol
  - Hypothyroidism
  - Liver disease, etc...

Keep in mind that macrocytic & microcytic anemias are most often anemias of decreased production of blood cells → so increased consumption of blood cells can only cause **normocytic anemia**!

Reticulocyte count

- Used to know if the normocytic anemia is caused by decreased cells production or by increased consumption of cells at the periphery/circulation.
- Reticulocyte formation the very last step before the formation of mature RBC.
- Reticulocyte cell is anucleated & has RNA that accounts for the blue colour in it.
- It is formed in the bone marrow and stored there for a while and then it gets released to the circulation and stays there for 24 hours until it expels the last content of its RNA and become a mature RBC.
- When blood cells are being consumed in the periphery, the bone marrow will detect that and start producing more RBCs but in this case, it doesn't give the reticulocyte enough time to stay in the bone marrow and it releases it early, allowing these reticulocytes to stay in the circulation for **more** than 24 hours.

  ➔ High reticulocyte indicates increased consumption of blood cells.

  ➔ Low reticulocyte indicates decreased production of blood cells.

These are some questions from the doctor's slides regarding this lecture

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 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 ➔ it is <u>Macrocytic</u>
E.G6PD deficiency

5. All are clinical manifestations of anemia of diminished production, except:

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

GOOD LUCK!