Blood composition, function and viscosity

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Blood composition

- Total Body Water (TBW) makes around 60% of total body weight,

TBW are composed of:

1-Extracellular fluid (ECF) that makes 1/3 of TBW

2- Intracellular fluid (ICF) that makes 2/3 of TBW

ECF is composed of:

1- interstitial fluid (that makes ¾ of ECF)

2- plasma (that makes ¼ of ECF), the average amount of plasma in adult human body with 70kg is 3L.

Plasma is composed of :

1- water (that makes 90% of plasma)

2- Inorganic sub (that makes 0.9% of plasma), inorganic sub composed of cations like Na+ (for osmolarity) and anions like Cl-, gases, miscellaneous substance: (glucose and vitamins), plasma lipids, and protein lipoprotein

3-Organic sub (that makes 9.1% of plasma),

organic sub is composed of plasma proteins (like Albumin, Globulin, Fibrinogen, Prothrombin).

All of these plasma proteins are synthesized by liver except gamma globulin which is synthesized by B-lymphocyte

As albumin is the most important protein to make osmotic pressure (pull fluid toward plasma), Albumin/Globulin must be in a fixed percentage (1.2 – 1.6) in normal condition.

As liver is responsible for producing Albumin, any problem of liver like cirrhosis will cause a reduction in albumin amount and a disturbance of osmotic pressure

Normally, excessive amount of albumin is excreted through kidney, so if there is a problem in the kidney like nephrosis, it will cause a reduction in albumin amount and a disturbance osmotic pressure.

As we said before, plasma is composed from a lot of proteins, one of them is globulin which has many subtypes:

1-Apha 1: like anti trypsin which is very important in pulmonology

2-Alpha2:such as Angiotensinogen

3-Beta type: coagulation factors transferrin

4-Gamma: such as antibodies

Normally, proteins in electrophoresis are arranged in specific order as albumin is the highest one (because it is the most abundant protein), then alpha 1, alpha 2, gamma, and finally beta. In renal acidosis, there will be a reduction in renin which result in storing angiotensinogen in higher amount without making angiotensin 1&2, and thus renal acidosis can be diagnosed by having higher amount of alpha 2 protein (there will be a huge gap between alpha 1 and alpha 2).

Blood volume

❖ Blood volume = The blood cells (which makes 3% of body weight) + blood plasma (makes 5% of body weight) =8% of our body weight.

To express Blood volume in Kg:

1- we multiply it with 70Kg: 8% × 70kg = to 5.6L = 5.6 kg

Blood Plasma =(makes 55% of Blood volume) 55% × 5.6L = 3L

Blood cell = (makes 45% of blood volume) 45% × 5.6L =2.5L

2- Total Blood Volume (TBV) = Plasma Volume / 1- Hematocrit (PCV)

- Total Blood Volume (TBV)= 2.8 / 1- 45%= 5.6L

❖ if you want to donate a blood you donate one pint or half a court (blood unit)= 500ml which should be less than 1/10 of your whole blood volume as we have around 10 pints (5L) in our body

* one quart/court = 2 pints.

❖ If you gave twice that you will lose a litre of blood, half a court of blood then you need a medical attention.

❖ So the person who less than 100 bound (less than 45kg) doesn't give blood as if he did he would donate more than 10% of his blood volume.

Function of plasma:

- Amino acid source
- Buffering (by anions like H_2CO_3)
- Blood viscosity 1.5 times than water resistance (by plasma proteins) to increase resistance and pressure.
- Coagulation (by fibrinogen + prothrombin)
- Defense Osmosis (by albumin)
- Transport molecules from and into the cell to regulate homeostasis and hemostasis

RBCS

Are synthesized either by : multipotent stem cell, erythropoietin (EPO)

- 1-Multipotent stem: produce different cells like Myeloid and lymphoid.

- Myeloid: produce proerythroblast ----> Normoblast ----> reticulocyte ----> erythrocyte (mature RBC)

mature RBC are Biconcave to flow smoothly in capillary as it has the ability (called RBC memory / variable diameter) to accommodate and change its diameter based on the structure they pass.

Hereditary spherocytosis : RBC will be in spherical shape due to genetic abnormality that makes it lose its ability to change the diameter (RBC memory), it will cause injury to endothelial cell.

RBC

- Rbc is Non nucleated, why?. bone marrow produce proerythroblast as a large cell with nucleus and mitochondria, but as maturation occurs, the cell decrease in size and start to lose it nucleus and organelles until it becomes erythrocyte (mature RBC with no nucleus and no mitochondria).

- RBC has short life span (120days) as it considered as untrue blood cells because it has no nucleus, and thus it has less ATP than true blood cells (like WBC), This is important as we can measure the amount of sugar in our blood using **Hgb A1C** (sugar hemoglobin)over 3 to 4 months

2- Erythropoietin (EPO)

- EPO function is to stimulate Bone marrow to synthesize RBC.

it is synthesized in Kidney (in higher amount) in interstitial cells of the peritubular capillary bed in the cortex in kidney
Liver (in lower amount)
Brain (in lower amount)

It is increased by:
hypoxemia, decrease O2 saturation, high altitude, left shift of hemoglobin dissociation curve.

* Cancer cells increase EPO like (Renal cell and hepatocellular carcinoma) in order to increase amount of RBC.

* In polycythemia vera (where there a lot of amount of RBC) we don't need to produce more RBC so it reduce EPO

* Some athletes inject artificial EPO to increase energy by increasing erythropoietin efficacy (increasing RBC amount)

Erythrocyte indices

1- RBCS count (Number)

- In Male = 4.5-6 million M/L In Female = 4-5 million M/L

2-Hgb Concentration (weight) = amount/ volume (g/dl)

in Male = 14- 17 g/dl (average 15 g/dl) in Female = 12-15 g/dl (average 13 g/dl)

3-Hematocrit (Hct) (volume) = Vol of RBCS/ Volume of blood

In Male = 45% in Female = 40%

4-Mean corpuscular volume (MCV) (size of RBC)

Normal RBC size(normocytic) = 80-100 fltomoter

If RBC was small cells (microcetic) < 80 = low MCV

If RBC was Large cells (macrocetic) > 100 = High MCV

Continue….

* Some diseases do not change the size of RBC as it remains normocytic, but there are some diseases that change it, like Iron deficiency anemia that makes RBC microcetic, whereas nutritional anemia like vit.b12 and folate definicy cause RBC to be macrocetic

5- Mean corpuscular hemoglobin (MCH) (average weight) = Average content of Hgb per red cells

- MCH= (Hb mass g/dl / RBC count /ML X 10 pictograms
- Male: 30 pictograms

6-Mean corpuscular hgb concentration (MCHC) (average density) = average content of Hb per unit volume of RBCS mass/volume density

MCHC= Hb/ Hct X100 Male: 33 g/dl

7- Red blood cells distribution width (RDW) = variation in diameter (Anisocytosis)

normally variation in diameter in RBC = 11.5-14.5%

if it elevated it means there are a disease (significant disease)

*RDW occur in nutritional anemia but does not occur in genetic diseases like thalassemia

Reticulocytes (baby erythrocyte)

It is arranged as a network of cells ,It can be differentiated from matured erythrocyte by having Large size with bluish cytoplasm, Normally it is present everyday in < 3% (1-2%) of blood

Splenic macrophage starts to Mature Reticulocyte every 24hrs

Anemia increase the number of reticulocyte as it stimulate EPO that stimulate bone marrow to make new erythrocytes (good response or efficacy erythropoiesis)

*Corrected reticulocyte count (CRC) = HCT/Normal hematocrit X reticulocyte count

*Additional correction of polychromasia (baby retics) CRC/2 = 2-3 days (it needs to make mature RBCS)

* The number in dominator (2) means reticulocyte needs two days to be matured, so each percentage of HCT has a specific time to be matured, and thus the number in the denominator can be changed according to HCT.

* CRC is used to know if someone has an anemia or not as CBC test does not differentiate between mature or immature erythrocyte.

Reticulocyte (continue…)

- CRC = (HCT (for the patient)/ normal HCT) X reticulocyte count

Example 1 : Retics index=3% HCT= 15% Normal HCT= 45%

CRC = (15%/45%) X 3 = 1%

1/2.5= 0.4 reticulocyte production index

The bone marrow is not putting enough retics (which means there is a problem in bone marrow as it can't produce 1-2% of retics)

Example 2: Retics index=18% HCT=15% Normal HCT=45%

CRC = (15%/45%)X 18% = 6%

6/2.5 =2.4

the bone marrow is putting enough reticulocyte (good response)

Anemia

Causes of anemia:

1-Decreased O2 carrying capacity of blood due to decrease Hb concentration (PaO2 and saturation of O2 in hemoglobin is normal)

2- Decreased total RBCs mass (due to hemorrhage)

3-Decreased Hgb, RBCs or Hct indicators

*RBCS nuclear scan to measure mass literally (very expensive test, not practical)

*Signs and symptoms of anemia:

Tired and pale, Dizziness, Dyspnea, Flow murmur and low viscosity of blood so it flow fast

Causes of Anemia

1-Survival defects:

A-Intrinsic defect (hemolysis)

1- If there is a defect in the Membrane so RBC lose variation in diameter (became spherical) = Spherocytosis (less surface area)

2- if there is an Enzyme deficiency (G6PD deficiency) which has a role in making ATP and NADPH as the latter has a specific role in reducing glutathione free radicals (H_2O_2) that is produced from fenton reaction, to prevent destruction of RBC, and thus increase the destruction of RBC

- NADPH is used also to convert methionine Fe^{+3} to Fe^{+2} through NADPH oxidase, NADPH oxidase also can generate superoxide from oxygen

3- if there is a defect Glycolysis: like deficiency in pyruvate kinase thay convert phosphopyruvate to pyruvate which produce 2ATP , if there was a defect in the enzyme then it increase 2,3 BPG that decrease O_2 binding affinity with Hb and it dissociate the curve to right shift, and thus produce less RBC.

4- if there is a defect in Hgb structure like in the DNA = sickle disease

Causes of Anemia

B-Extrinsic attack (hemolysis) RBCs, like:

- Sequestration (hypersplenism) in portal hypertension, as spleen has a higher activity so it destruct more RBC
- Blood loss (hemorrhage) in peptic ulcer disease (in chronic inflammatory disease)

1- Production defect : if there is a defect in bone marrow or kidney damage (EPO), so it makes low reticulocyte

2-Maturation defects, if there is a defect in Hgb: Iron , globin, DNA