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carbohydratesisomersketone starchlipidproteinamine

Bio chemistry

Doctor 2017 | Medicine | JU

Sheet Slides

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DOCTOR

Dr.Nafez

What is biochemistry?

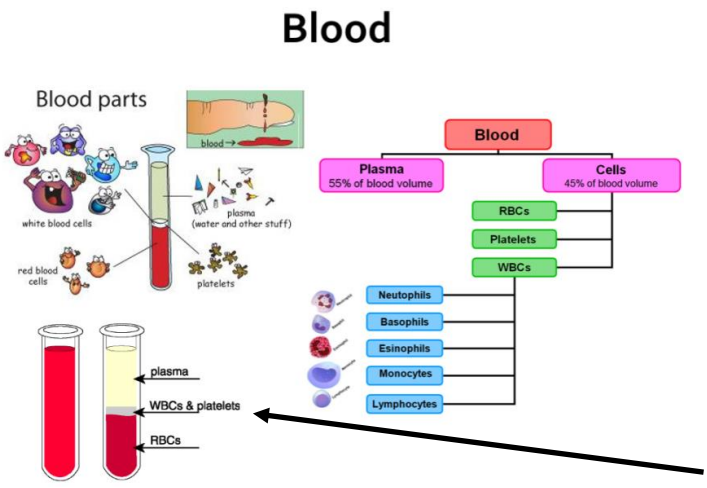
It's the chemistry inside living cells.

Biochemistry consists of the structure and function of macromolecules (in the previous semester we talked about the structure. In this semester we will be discussing the related function of each molecule).

All macromolecules end up as **acetyl coA** when the body breaks them down for energy. This acetyl CoA enters Krebs cycle → oxidative phosphorylation→ to provide ATP.

***So, all macromolecules produce energy (but not the same amount) for example 1 molecule of Fat produces **twice** as much calories as 1 molecule of sugar (9 kcal/gm vs 4 kcal/gm) when burned.

1. **What is plasma, and how can we extract it?**
2. **What are the different components of plasma?**



Blood is made of 2 components:

1) Plasma (briefly speaking, it's the liquid that cells are suspended in).
2) Cellular component:
RBCs (erythrocytes)
WBCs (leukocytes)
Platelets

NOTE: we call the mixture of WBCs and platelets "Buffy Coat"

"cells are suspended in plasma" What does that mean? Does the word "suspended" mean anything in biochemistry?

It means that the cells are not soluble, and they stay hanging in plasma.

How to separates the 2 components of blood?

1- Precipitation ➔ (by leaving the blood sample for an hour). It's the circulatory movement of the blood that keeps cells suspended.

2- Centrifugation: a technique which involves the application of centrifugal force to separate particles from a solution. In this case, to divide the blood into it's main components based on their density, size and shape.

NOTE: Since the cells are suspended in plasma, leaving the blood sample for ≈ 1 hour in normal conditions would separate it to form 3 layers:

RBCs at the bottom, liquid plasma at the top, and in between WBCs (the buffy coat).

NOTE: WBCs are good as a diagnostic and research tool, since white blood cells are the only cells in blood that contains a nucleus and DNA. Because of that any mutation can be known by taking a blood sample and examining the WBCs.

FURTHER EXPLANATION :(not mentioned by the Dr. but it's just a reminder of what we studied previously):

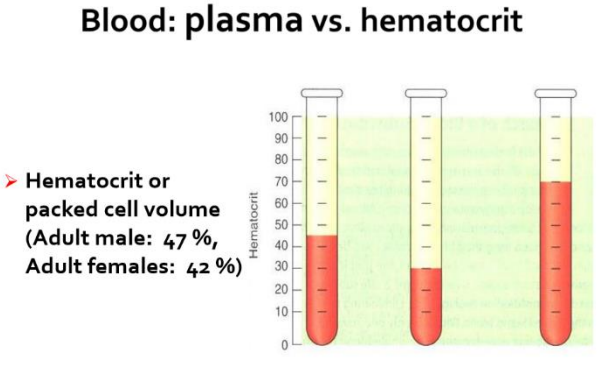
The process of gene expression is used by all known life—eukaryotes (including multicellular organisms), prokaryotes (bacteria and archaea), and utilized by viruses—to generate the macromolecular machinery for life.

Several steps in the gene expression process may be modulated, including the transcription, RNA splicing, translation, and post-translational modification of a protein. Gene regulation gives the cell the control over structure and function, and is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism. Gene regulation may also serve as a substrate for evolutionary change, since control of the timing, location, and amount of gene expression can have a profound effect on the functions (actions) of the gene in a cell or in a multicellular organism.

Hematocrit OR Packed cell volume:

The hematocrit blood test determines the percentage of blood cells in a given sample.

Note: on the internet you may find hematocrit as the percentage of RBCs only (its true that RBCs make the majority of cells but it is better to



say that hematocrit is the percentage of all cells not only RBCs).

hematocrit percentage in males =47% while in females it = 42%

Any change (increase or decrease) on these percentages means that there is a pathological condition.

For instance, in anemia we would find the percentages lower than the ones above.

ESR:

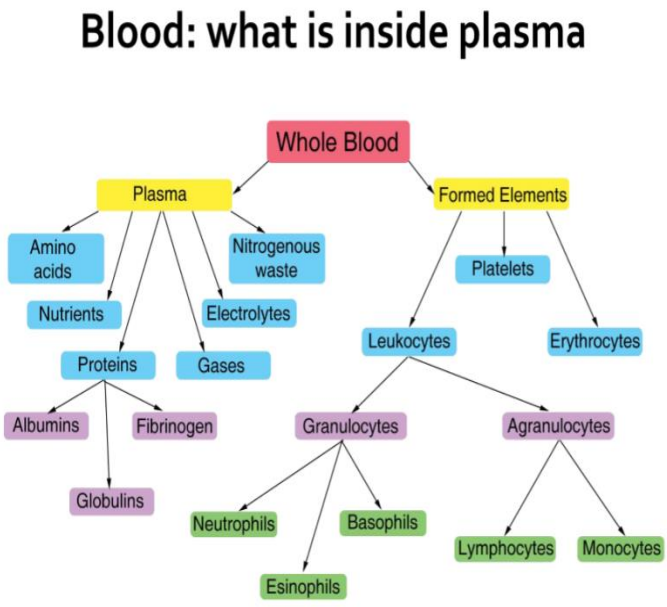
ESR or erythrocyte sedimentation rate is a previously used diagnostic test (widely used before the advanced diagnostic tests because the new ones are more specific). This test is based on the nature of blood. It measures the rate at which RBCs precipitate (sediment).

It was as simple as this, a blood sample would be kept to rest for an hour (any increase or decrease on that time is a marker for a disease). For example, cellular inflammation results in fast precipitation. Sometimes the change in the rate would be a normal physiological condition as in (pregnancy it precipitates in less than 1 hour).

****REMEMBER, it's not a specific test.

Plasma:

As the Doctor said it is composed of everything Since it's the main way of communication between organs and the outside environment. Its responsible for messages from the blood to everywhere (anything that is found in cells or what cells need will be there. For example, metabolites/ wastes/ water/ nutrition / gases/ electrolytes).



Its composed of 92% water 8% solids

Plasma

- Liquid medium where cells are suspended
- Composition: ▪ Water (92%) ▪ Solids (8%)
  - Organic:
    - Plasma proteins: Albumin, Globulins & Fibrinogen
    - Non-protein nitrogenous compounds: urea, free amino acids, uric acid, creatinine, creatine & NH_3
    - Lipids: Cholesterol, TG, phospholipids, free fatty acids
    - Carbohydrates: Glucose, fructose, pentose
    - Other substances as: Ketone bodies, bile pigments, vitamins, enzymes & hormones
  - Inorganic: $Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, HPO_4^{2-}, SO_4^{2-}$

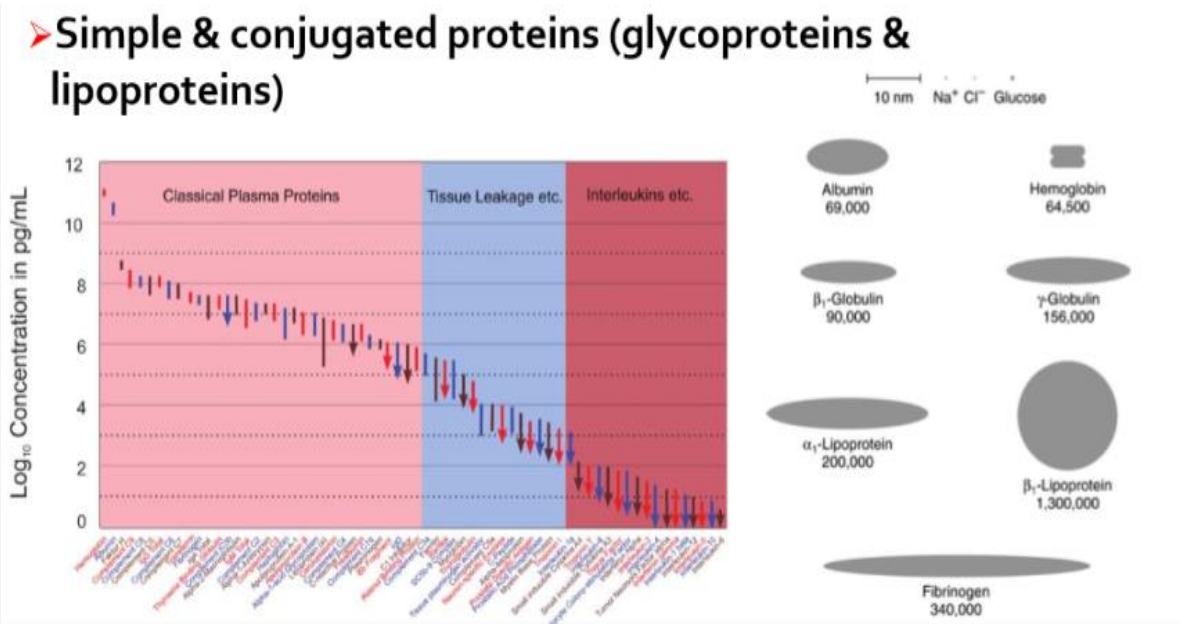
There are more than 500 kind of plasma proteins (this number was figured out using the latest advanced techniques of discovering proteins).

NOTE that most of the plasma proteins are modified (conjugated to either lipids or carbohydrates).

Proteins make up about 6-8 grams per deciliter (0.1 liter or 100 ml). Main types are albumin, fibrinogen and globulins (alpha1, alpha2, beta and gamma proteins)

Proteins differ in MW and their shapes. For instance, Hemoglobin is 65K Daltons while albumin is 69k Daltons (the shape of the protein is so important and has a huge effect).

- Simple & conjugated proteins (glycoproteins & lipoproteins)



Separation of plasma proteins (2 techniques):

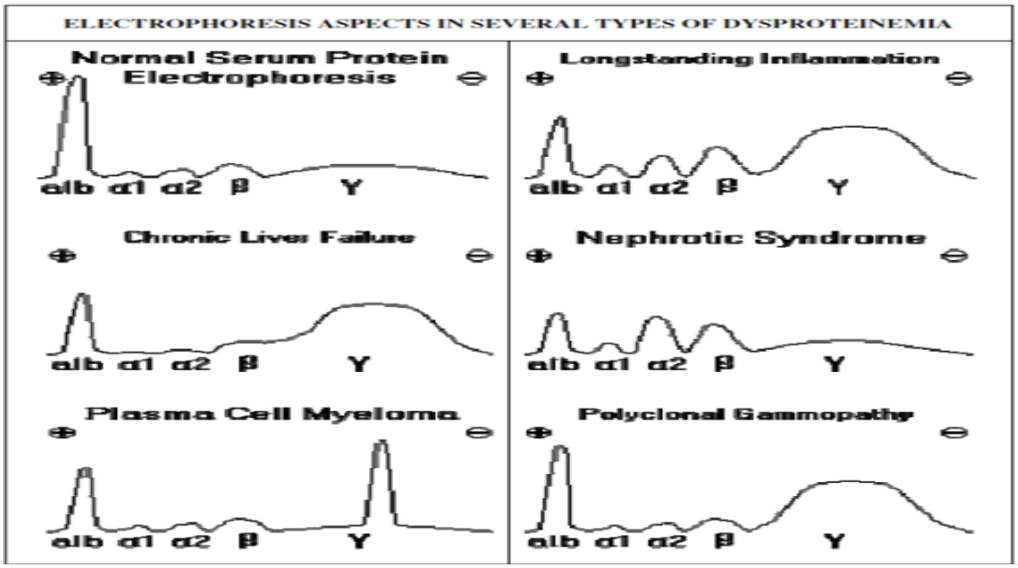
1- Salting out: is the precipitation of proteins depending on their solubility, salts solubility is higher than proteins solubility in water (to be more soluble means to have more affinity) so when salts are added they become surrounded by what's called the hydration shells. In other words, the water interactions with salts are stronger than the interactions with proteins. Therefore, water gets away from proteins and the proteins start interacting with each other, which leads to aggregation and precipitation.
   ⇨ The lower the solubility of a protein, the earlier it will precipitate (and vice versa).
2- Gel electrophoresis:
   The serum (plasma without clotting factors (mainly fibrinogen)) is added to the wells and the plasma proteins (SDS added to make a uniform negative charge) will result in 5 bands including albumin, alpha1, alpha2, beta and gamma proteins. The fastest protein is albumin since it has the lowest MW and its the most negative (DR said that the main reason is MW since the SDS results in uniform negative charge).
   ⇨ We didn't use not plasma because when plasma is added to the well its exposed to air and that leads it to coagulate.

   results of electrophoresis are 5 bands:

   - **Albumin**
   - **α band:**
     - ✓ **α1 region consists mostly of α1-antitrypsin**
     - ✓ **α2 region is mostly haptoglobin, α2-macroglobulin, & ceruloplasmin**
   - **β band: transferrin, LDL, complement system proteins**
   - **γ band: the immuno-globulins**

   1) Each band represents a group of proteins (only albumin band contains 1 protein).
   2) There is beta 1 and beta 2 but it needs longer time to separate, gamma proteins don't separate at all. (alpha 1 and 2 have approximately the same MW).

3) Gamma globulins are immunoglobulins (antibodies) and there are 5 types of antibodies (IGG,IGM,IGA,IGD,IGE). Gamma globulins are the only ones made by mature B lymphocytes (mature B lymphocytes are called plasma cells), the rest of plasma proteins are made in the liver.
4) Densitometer measures the thickness of the band and convert it to a curve.
5) Concentrations (albumin>gamma>alphas and the beta)
6) Albumin makes (50% to 60%) of the 6-8 grams plasma proteins which means it is approximately (3.5-5.5 g/dl).
7) 90% of the Alpha 1 band is the alpha1-antitrypsin protein.



The DR said that we should be able to predict what happens to the graph when particular changes happen. (liver or kidney failure, cancer or inflammation).

EXAMPLES:

In the case of inflammation globulins concentration increases in the body. (1st graph to the right)

Renal failure (filtration failure or nephrotic syndrome) in urine analysis will show that some proteins were lost from the blood (note that in this case the lost is not selective to any specific type of protein.

Liver failure (alcoholic liver, cirrhosis, fibroses hepatitis) since the liver is responsible for the production of all proteins except gamma globulins their percentages will come down.

plasma cells with Cancer (mature B lymphocytes) gamma globulins will rise (we have 2 cases, the 1st one happens when only one type of proteins increases, we will have a sharp increase in the graph, 2nd is that all 5 gamma were effected, we will notice a broad increase in the graph). The two cases are represented by the last two graphs in the diagram above.

Most of the plasma proteins are made inactive (preproproteins) and they are modified later, this is done for 2 reasons: 1st no need for the protein to function unless its needed (it will be activated later as in fibrinogen). 2nd if the site of synthesis differs from the site of function.

It takes from 30 mins up to several hours from the beginning of synthesis until it becomes mature and functional.

All plasma proteins are glycosylated except for albumin (carbohydrates are important to improve solubility, communication and attachment). But in the case of albumin if it was glycosylated its solubility increases and because albumin is the most abundant protein it will have a huge impact on the blood so it becomes denser (viscosity increases) and harder to move.