

DOCTOR 2020 | JU

METABOLIS

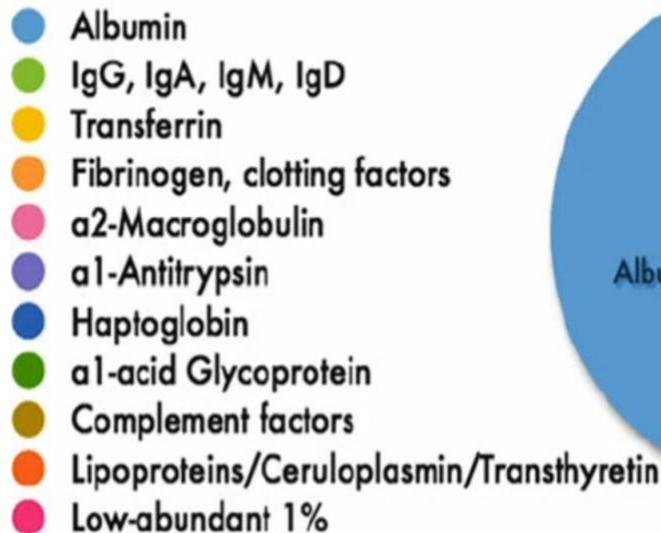
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Plasma Proteins

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❖ what is the meaning of metabolism?

- The degradation and building up of macromolecules (proteins ,nucleic acid, lipids and carbs)
- While the biochemistry was about the structure and function of macromolecules .

❖ Why are the macromolecules being degraded?

- To supply us with energy
- But when we don't need energy they get stored in the body as fat, glycogen ...etc
- **So in general the energy is stored in our bodies in the form of BONDS .**
- In the case of starvation our body start degrading everything in order to energy .
- Nitrogenous containing compound is a term of proteins and nucleic acids .

- ❖ **What is the definition of the plasma?**
 - The liquid component of the blood where cells are suspended
- ❖ **How can we get it out of the blood simply ?**
 - By leaving it
- ❖ **What is the difference between the terms suspension and solution ?**
 - Suspension where the materials are not dissolved, so if we leave it for a while it will precipitate.
 - Solution where the solutes are dissolved
- ❖ **What are the cells of the blood?**
 - RBCs (erythrocytes) the major cells of the blood (can sediment over time at a normal rate)
 - The rate at which the RBCs are being precipitated is called **Erythrocyte Sedimentation Rate (ESR)** which increases and decreases in certain conditions
 - Platelets
 - WBCs
- ❖ **What are the cellular part of the blood called ?**
 - Formed element
 - If we take a 100 ml of the blood ,the cellular part will count for 45% of the volume while 55% is for the plasma (it differs between adult males, females and children)
- ❖ **What we call the precipitated part of the blood ?**
 - It is called **Haematocrit** or **packed cell volume**
 - Haematocrit ,packed cell volume, cellular part of the blood and formed element all are referring to the same thing .
- ❖ **What plasma includes ?**
 - ❖ It contains everything .
 - ❖ The blood communicates with the whole body ,it is the interface between inside and outside ,so it should include everything that your body either needs or secretes out

- ❖ **How many plasma proteins do we have ?**
 - Over 500 (detecting by biochemical techniques)
 - Most of them are in frequency, the concentration of them is very low .
 - Few of them have a high concentration.
- ❖ **There are three main classes of plasma proteins ?**
 - 1.Fibrinogen** (responsible for the clotting process of the blood
 - 2.Albumin** (the major one, it is small with the highest concentration)
 - 3.Globulin**
 - We can get the plasma either by leaving it or by centrifugation.
 - We can extract the plasma proteins by different biochemical techniques that we have discussed last semester
- ❖ **One of these techniques is called salting out ,so what is it ?**
 - Increasing the concentration of salts which will compete with the protein for water which will bind the salts leaving proteins, because they have better solubility ,so it depends on the concept of solubility .
 - Out of the salting out techniques we get the three classes of the plasma proteins
- ❖ **Can we use the gel electrophoresis for the plasma and why?**
 - **No**, because of the presence of the fibrinogen (clotting factor)
 - So we use something called **Serum (plasma without fibrinogen)** so it is called as defibrinated plasma
 - Now ,If we run the serum on the gel electrophoresis we get only 2 classes of proteins (globulin and albumin)
 - The **gel electrophoresis** ,it provides a better technique for separation of proteins that the **salting out** ,because the last gives as a crude collection of proteins (not separ.)

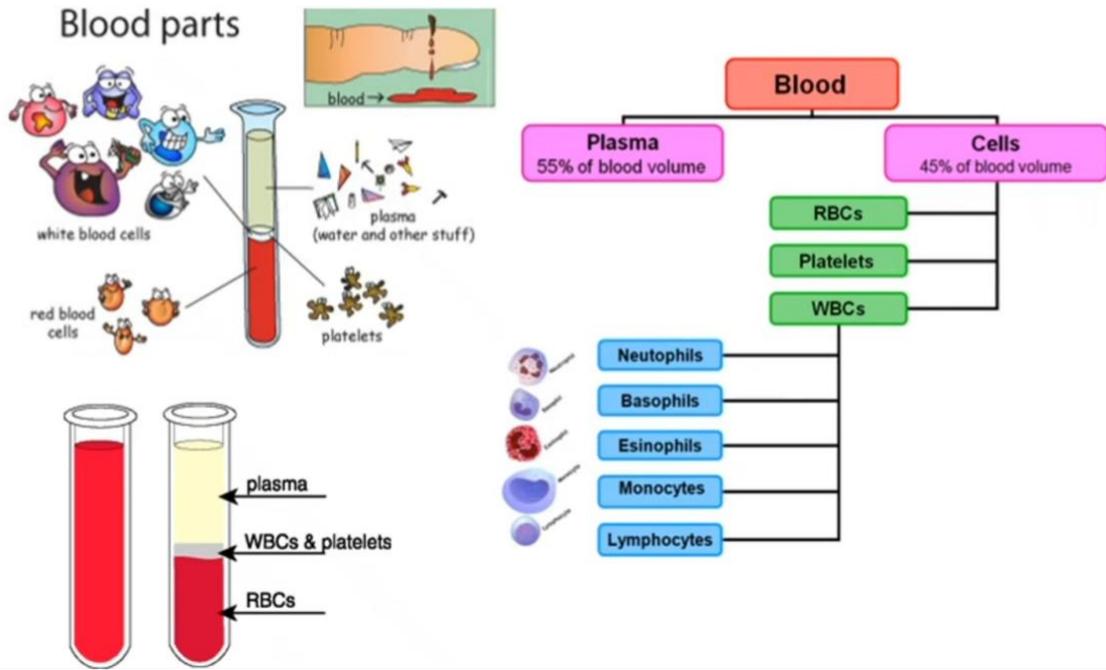
- Then according to the molecular weight (the main criteria of separation on this technique) , the albumin was the smallest so it migrates the fastest
- The bounding of the plasma proteins to other things like sugars or lipids changes the molecular weight ,so the speed of migration of that protein (conjugated)
- Also we care about the structure of the protein if it monomeric , dimeric ,trimeric or more than that .
- Each band in this technique indicates a class of plasma protein
- They called the bands of the globulin class as **alpha ,beta and gamma band.**
- The **alpha band** separates easily into two bands ,they call them a1 and a2
- The **beta band** needs more time and better separation method in order to give you two bands as well, and the gamma will still by itself .
- **The gamma globulin are the immunoglobulins (antibodies)**

What should we know?

1. What is plasma, and how can we extract it?
2. What are the different components of plasma?
3. Plasma proteins (general functions, basis of classification, associated processes and molecules)
4. Plasma proteins: (structure, synthesis, function & diseases associated)

Albumin & pre-albumin	α 1-antitrypsin	Haptoglobin (Hp)
α 1-fetoprotein (AFP)	Ceruloplasmin	C-Reactive Protein

Blood



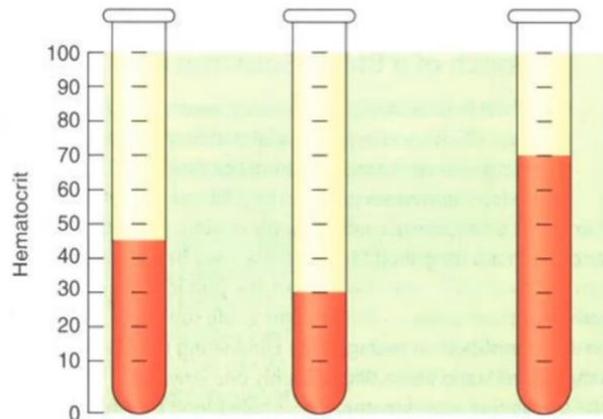
- Generally speaking the blood either cells or plasma
- Cells constitutes for 45% while the plasma 55%

Blood: plasma vs. hematocrit

➤ **Hematocrit or packed cell volume**
(Adult male: ~47 %, Adult females: ~ 42 %)

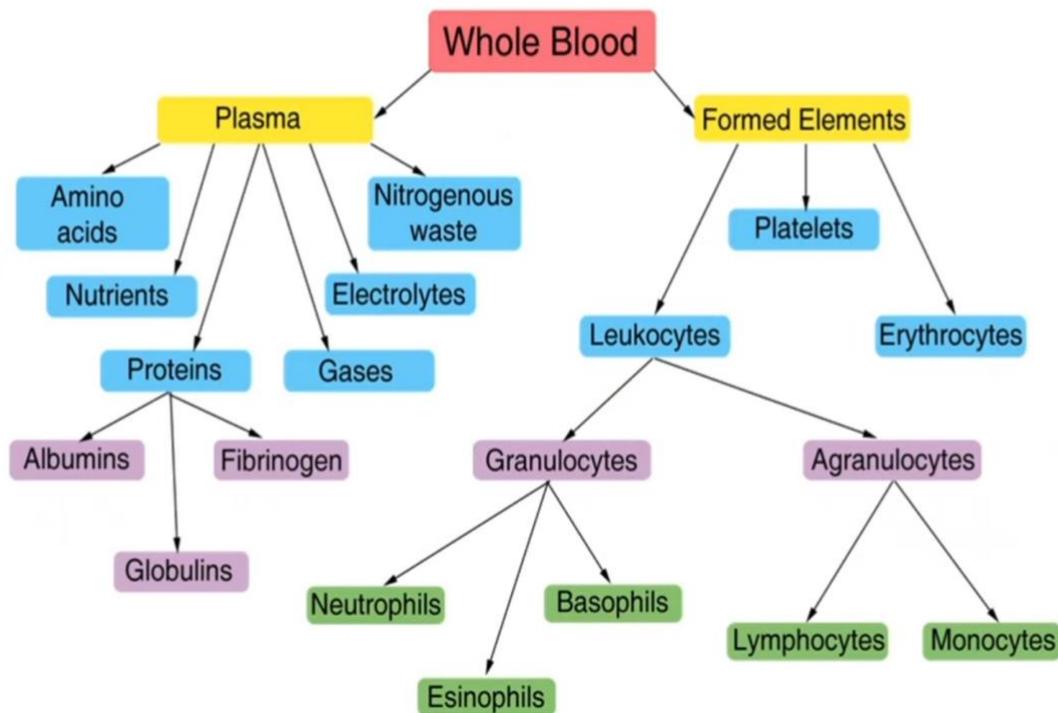
➤ **Ranges:**

- 36% to 48% for women
- 42% to 52% for men
- 30% to 44% for children, depending on age



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Blood: what is inside plasma

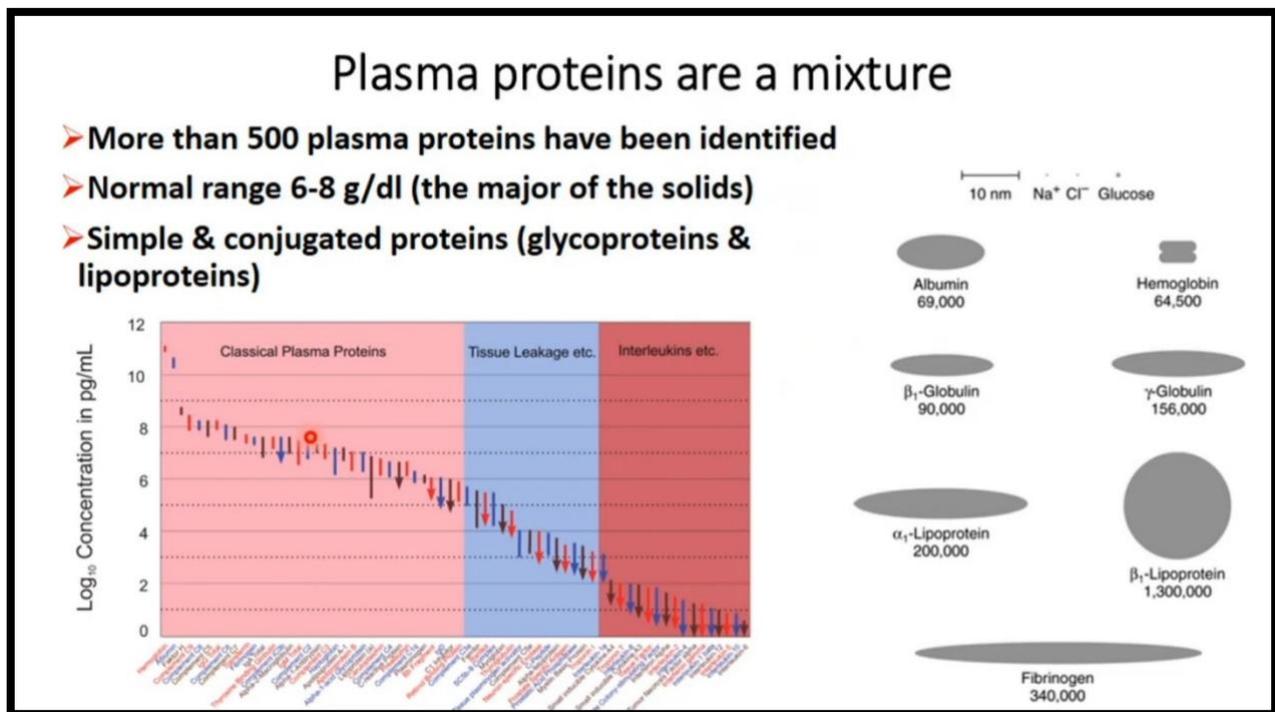


- Again the blood consists of cells and plasma
- And we are concerned here in studying the proteins of plasma

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 & NH₃**
 - **Lipids: Cholesterol, TG, phospholipids, free fatty acids**
 - **Carbohydrates: Glucose, fructose, pentose**
 - **Other substances as: Ketone bodies, bile pigments, vitamins, enzymes & hormones**
 - **Inorganic: Na⁺, K⁺, Ca²⁺, Mg²⁺, Cl⁻, HCO₃⁻, HPO₄²⁻, SO₄²⁻**

- The solids can be organic or non organic , the proteins are out of organic

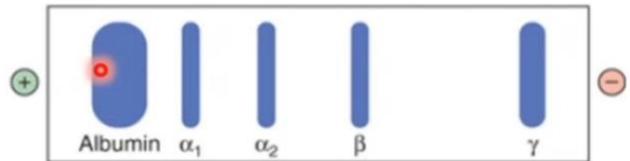


- **How much is the dl? it is 100 ml**
- **Deci is one tenth of the unit**
- Almost 60% of the plasma proteins is the albumin , which is about 4g/ dl
- **Few** of them are **simple** which means that they are not bound to anything ,they do their function through amino acids only .
- **Most** of them are **conjugated** to other things **mainly lipids and carbohydrates.**
- **Small** number of them are bound to **lipids (lipoproteins)** and **most** of them are **bound to sugar (glycoproteins)**
- **Bound to sugar = glycosylated**
- The **haemoglobin** is only for **reference** , it is not a plasma protein because it is present inside **RBCs** not in the **plasma**
- The molecular weight of albumin is close to that of the haemoglobin but its shape differs .
- The shape of albumin is ellipsoidal ,but fibrinogen is elongated

Separation of plasma proteins

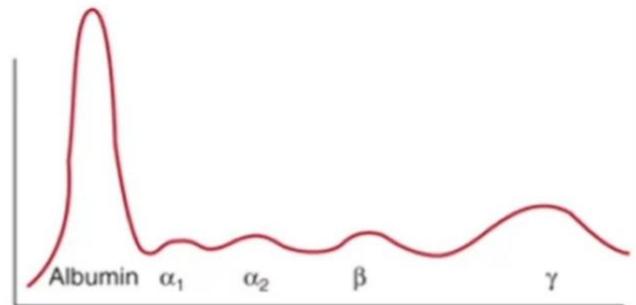
➤ **Salting-out (ammonium sulfate):
fibrinogen, albumin, and globulins**

➤ **Electrophoresis (most common): serum
(defibrinated plasma), five bands
(albumin, α_1 , α_2 , β , and γ)**



NORMAL VALUES:

Name	Absolute values (g/l)	Relative values (%)
Albumins	35 – 55	50 – 60
α_1 -globulins	2 – 4	4.2 – 7.2
α_2 -globulins	5 – 9	6.8 – 12
β -globulins	6 – 11	9.3 – 15
γ -globulins	7 – 17	13 – 23

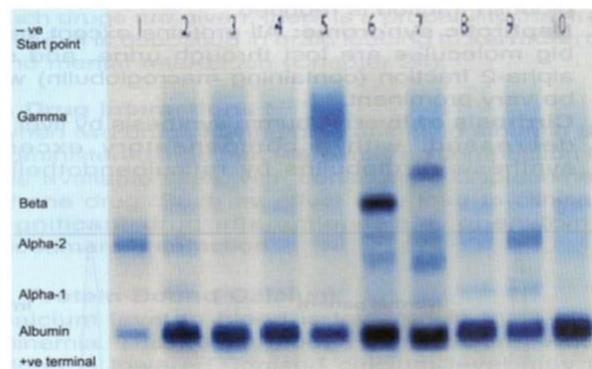
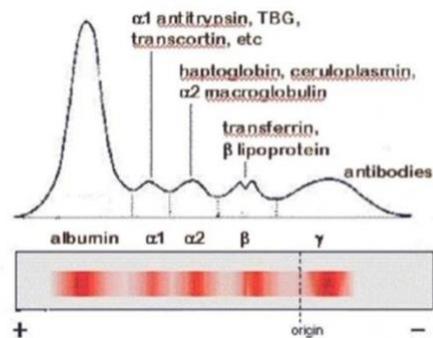


- We notice from the results of the gel electrophoresis that the **Albumin** band is the **major** band
- The **density** of band indicates the concentrations ,so that the **albumin** has the **highest concentration** .
- The instrument that **measures the density** of the **bands** is called **densitometer** , we put the gel inside it.
- The albumin has the highest peak represents it highest concentration .
- **α_1** , **α_2** and **gamma** bands are not single proteins ,each band of them represents a collection of proteins close to each other in their molecular weight .
- **90%** of the proteins that are within **alpha1** band is about single protein called **a1 antitrypsin** or **a1 anti proteinase**

□ لا حول ولا قوة إلا بالله العلي العظيم

Electrophoresis of plasma proteins

- Albumin is smaller than globulin, and slightly negatively charged
- Globulins (3 bands):
- **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

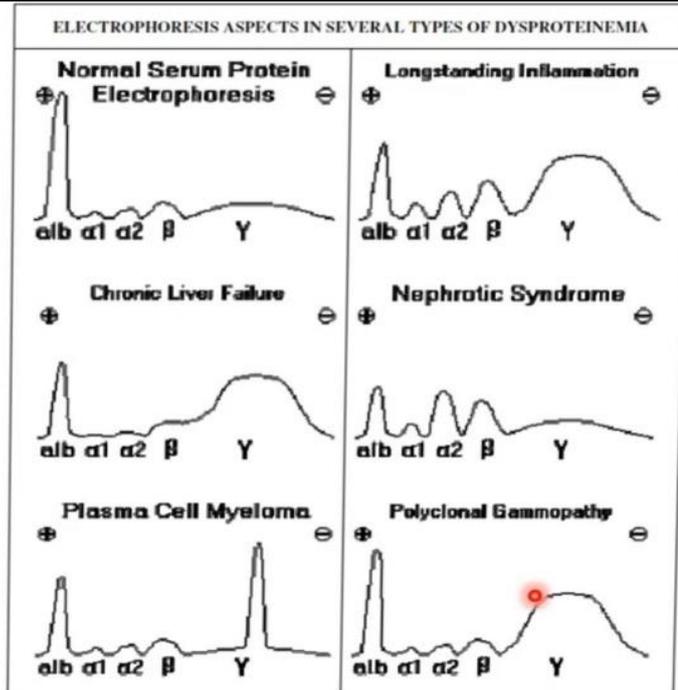


- As you can see, that **alpha2 band** is consisted from more than one protein
- The **transferrin** protein in **beta band**, is the one that is responsible for carrying the **iron** inside the blood
- ❖ How many types/clones of the **immuno-globulin** do we have?
 - 5 **different** types by the amino acid sequence
 - **so** they don't have the same molecular weight, but close to each other as **monomers**, that is why they form a one band
 - **because** they are 5 **different** proteins, they form a **wide** band
 - In the case of inflammation, the concentration of the antibodies or one of them would increase, so the curve of the gamma globulin in the site of that antibody would be sharp (sharp peak)

- If I'm telling you that most of the plasma proteins, except for the albumin are increased dramatically in their concentration ,in the case of chronic disease ,chronic inflammation , cancer ,trauma ,it will be indicated as an increase in the conc. of all of them except for the albumin it would still be the same .
- Most of the plasma proteins are being synthesized in the liver except for two groups of proteins, which **are the antibodies they are synthesized in the matured B lymphocyte (plasma cell) in the bone marrow, other groups are synthesised in the endothelial cells .**
- ❖ **If we have a cancer affecting one type of the Ig (more than one type of cells producing antibodies) then we would have a sharp peak for the antibody, but if it affects more ,then we would have a wide increase in their concentration collectively**
- ❖ **In the case of the liver failure, the concentration of all proteins would be decreased, except for the immunoglobulin, it might be increased because of inflammation and other causes .**
- ❖ The function of the **kidney** is to **collect** and **get rid** of the **wastes** in the blood, almost **180L** of blood is being filtered by kidney per day, but only **1L is excreted** outside in the form of urine
- ❖ In the case of **kidney failure**, the concentration of all proteins would be **decreased**, because the proteins would be excreted out .

سبحان الله والحمد لله ولا إله إلا الله والله أكبر"

Clinical Cases



- Nephrotic syndrome is a renal failure
- Plasma cell myeloma is a cancer affecting one type of antibodies (sharp peak)
- Polyclonal Gammopathy is a cancer affecting more than one type of antibodies (wide peak)

Synthesis of plasma proteins

- Mostly liver (albumin, globulins), γ -globulins (plasma cells; lymph nodes, bone marrow, spleen)
- Most plasma proteins are synthesized as preproteins (signal peptide)
- Various posttranslational modifications (proteolysis, glycosylation, phosphorylation, etc.)
- Transit times (30 min to several hours)
- Most plasma proteins are Glycoproteins (N- or O-linked). Albumin is the major exception

🕌 اللهم صل وسلم وبارك على سيدنا محمد وعلى آله وصحبه أجمعين 🕌

- ❖ Most of the proteins are synthesized in the liver except for Ig (plasma cell) and another one in endothelial cells .
- ❖ Most of them are synthesized as pre pro proteins because they are synthesized in tee liver but should function in the plasma ,so they are synthesized in their inactive form .



غراس الجنة:

- سبحان الله

- الحمد لله

- لا إله إلا الله

- الله أكبر

- لا حول ولا قوة إلا بالله