University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Biochemistry

● Sheet ○ Slides

Lecture #: 1 Date: 15/9/2013

Title: Plasma protiens

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Price: .....

PLASMA PROTIENS

Refer to slide #1

* Goals from these 2 lectures:

1)What is the plasma? How can we get it?

2)What are the different components of the plasma?

3)What are the plasma proteins ,their functions generally and specifically and processes associated with these proteins?

4)Different types of plasma proteins:

–Albumin & prealbumin

–α1-antitrypsin

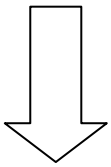
–Haptoglobin (Hp)

–α1-fetoprotein (AFP)

–α2-Macroglobulin

–Ceruloplasmin

–C-Reacrive Protein



Those are the main proteins that will be discussed,we will also discuss their structure,how they are getting synthesized,function and associated diseases when they are not there or when they are in excess.

****BLOOD** refer to slide #2

Blood is generally composed of :

1)Plasma

2)Cells: a)RBCs

b)platelets

c) c)WBCs :

- Neutrophils
- Eosinophils
- Basophils
- Monocytes
- Lymphocytes

**What is the plasma?
It is a liquid part where blood cells are suspended in

NOTE: Anything except cells is plasma

**How can we get plasma and cells?

By centrifugation or by leaving them alone and then after a while the cells will precipitate

This is a test done in hospitals called erythrocyte limitations rate (ESR)

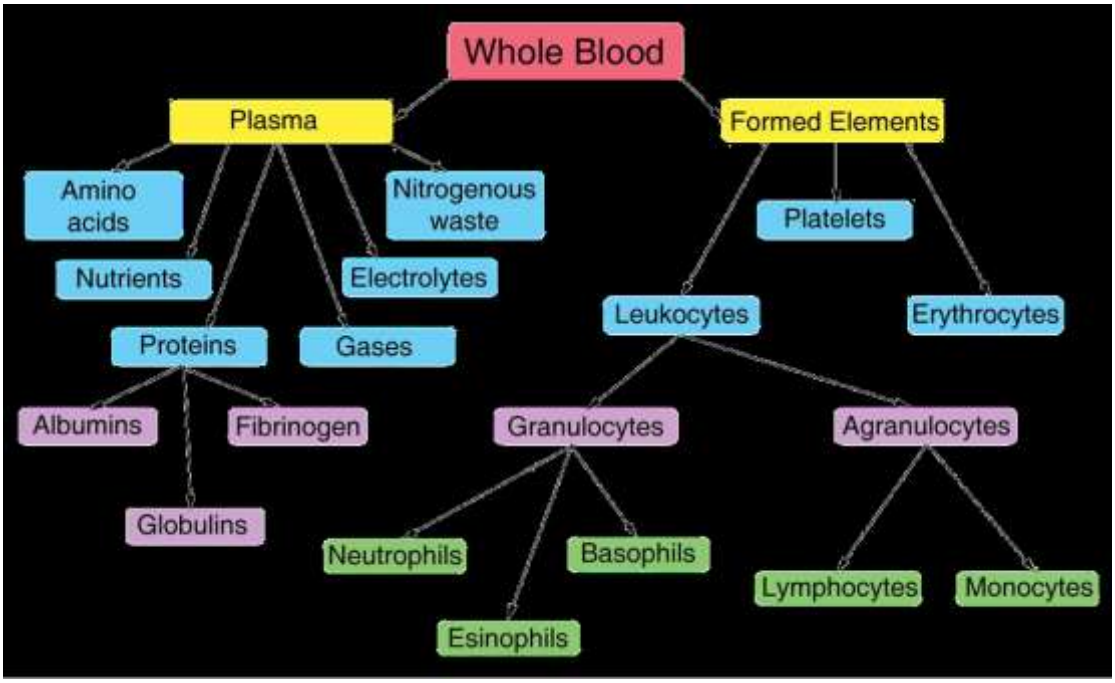
""High rates of this test are found during pregnancy and inflammation""

- During this test the cells precipitate , by this we conclude the time needed for precipitation and percentage of these cells in the whole part, usually the cells constitute 45% of the total volume of blood and 55% for the plasma .

Refer to slide #3

Hematocrit or packed cell volume (ESR)
**How much cells precipitate over time in a blood sample?
Percentages: In males :47%
In females : 42%

Refer to slide #4



This slide contains general information , we mentioned previously that blood consists of cells, we talked about them and their subclasses in general .

**What are the components of the plasma?

As we said, the plasma is the liquid part where cells are found, so anything except cells will be found in the plasma like :

1)Nitrogenous waste such as urea and ammonia, we can find them in percentages in the blood.

2)Electrolytes:sodium (Na+),potassium (K+),chloride (Cl-)

3)Gases:Dissolved CO2 , dissolved oxygen

4)Proteins:Plasma proteins (albumin,globulins,fibrinogen)

5)Nutrients:glucose

6)Amino acids that are broken down from proteins or absorbed through intestines.

Refer to slide #5

Plasma is mainly composed of water 92% and 8% solids (Nitrogenous waste, Electrolytes, Gases, Proteins, Nutrient , Amino acids)

##solids are anything except water##

- ❖ Solids are divided into:

1)Inorganic: Na+,K+,Ca2+,Mg2+,Cl-,HCO3-,HPO42-, SO42- (Electrolytes)
2)Organic:they are divided into :
a)Protein part:

Plasma proteins: Albumin, Globulins & Fibrinogen

Non-protein nitrogenous compounds: urea, free amino acids, uric acid, creatinine, creatine & NH3

- o Where is the uric acid high?

  In Gout داء النقرس

Lipids: Nutrients transported through blood (Cholesterol, TG (triglycerides) , phospholipids, free fatty acids)

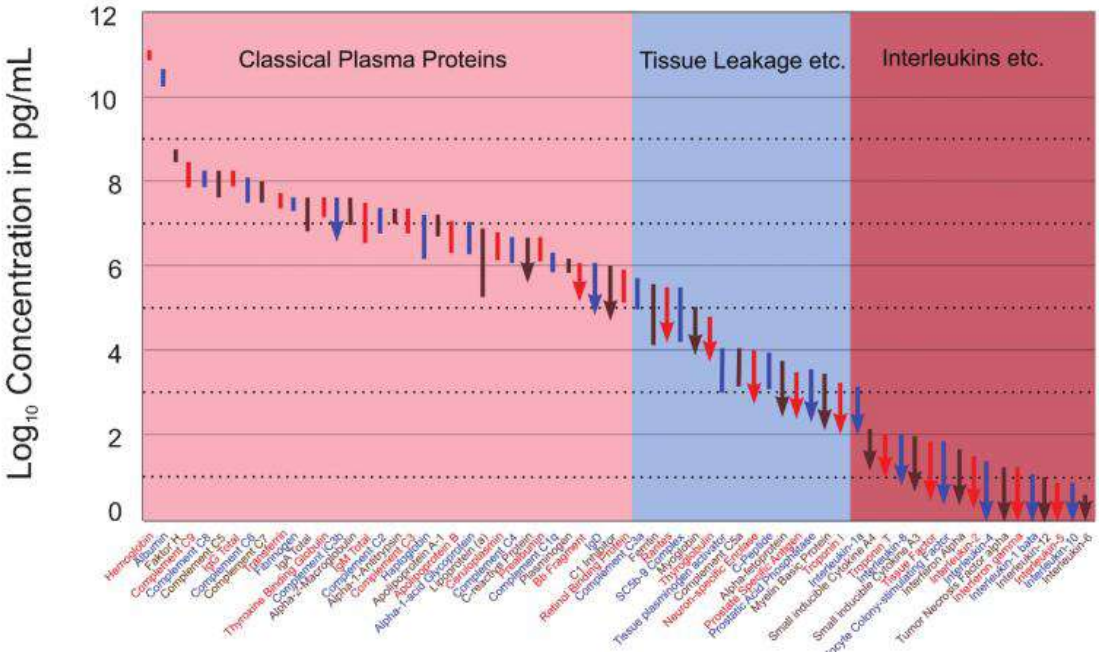
Carbohydrates:(Glucose, fructose, pentose) they are present as nutrients in the blood (within plasma)

Other substances as: Ketone bodies, bile pigments, vitamins, enzymes & hormones

*what is bile pigments (الصبغة الصفراء)??
They are found in the gallbladder , formed by the liver and stored in gallbladder to be secreted into the intestines to facilitate absorption and digestion of lipids then they undergo reabsorption and return to the circulation and then to the liver.

Refer to slide #6

How many proteins do we have in the plasma? Very high number



The x axis represents proteins found in the plasma(these are the proteins identified until now)

- The normal range of proteins is 6-8 g/dl (this range is for all proteins not for a specific class)
  *g=gram *dl=deciliter

  *Plasma proteins can be simple which means that they can work by themselves or conjugated(attached to other components so that it will be active)
  *Most of the plasma proteins are glycoproteins with some **exceptions** such as albumin which is simple,not conjugated ,not attached to carbohydrates and it can work by itself ,other plasma proteins can be lipoproteins(apolipoproteins) they are used in transportation of lipids through the blood.

  - ✓ REMEMBER:glycoproteins are proteins attached to carbohydrates .

- Main proteins found in the plasma:
  1)Hemoglobin(we will talk about it in details in the third year)
  2)Albumin
  3)Globulins (α , β, γ)

**What are the γ-globulins?
They are antibodies (immunoglobulins)

4)Fibrinogen :It is very important why? Because it is one of the main clotting factors found in the blood .

Refer to slide #7

**How can we get the main parts of the plasma proteins,how can we get them out of the plasma?

By purification, two main techniques are used :
1)Salting out :
When we increase the amount of salt inside the plasma sample ,the proteins start to go out gradually and by this **fibrinogen,albumin and globulin** precipitate, three main classes precipitate at different times so we find fibrinogen,albumin and globulin.
globulins go down together in one group (α , β, γ) because their structures are close to each other and they almost have the same size and same charge so that's why they precipitate together.

2)Electrophoresis: it is done on the charges
*We can't do electrophoresis on a plasma sample instead it is done on serum
*we can't put a plasma sample containing a lot of clotting factors ,if we put it in electrophoresis inside gel it will clot and block the gel (won't move) so we have to remove the clotting factors from the plasma .

- What do we call the plasma without clotting factors? Serum
- What is serum?It is defibrinated plasma which means that we have removed everything related to fibrin which is the main part of clotting factors.

*Fibrinogen (inactive) ⟹ Fibrin(active)

*When we do electrophoresis on a serum sample everything will go out except fibrinogen

EXAM QUESTION: electrophoresis is done on a **serum** sample,all of these will go out of the sample except :***FIBRINOGEN***

❖ What do we get when we do electrophoresis?
1) band Of the albumin
2)α -globulins divides into 2 parts α1, α2
3) β if it continues in the electrophoresis for a long time it divides into β1 β2 which mainly goes out as one band
4) γ-globulins which are antibodies found in the plasma

**Albumin is mainly negatively charged, it has the smallest size of all plasma proteins , so because of its negative charge and small size it will be the fastest one moving towards the positive electrode.In a serum sample the albumin is the fastest one migrating towards the positive electrode then (α , β, γ) arranged according to the bands in the gel.

**Albumin is the main part of the plasma proteins ,it is important in the transportation of nutrients and drugs (drugs that are given to patients mostly attach to albumin which transports them to the parts of the body).

✓ ***YOU HAVE TO KNOW THAT THE ALBUMIN HAS THE HIGHEST PERCENTAGE AMONG PLASMA PROTEINS & CONSTITUTES ABOUT 6O% OF THE PLASMA PROTEINS***

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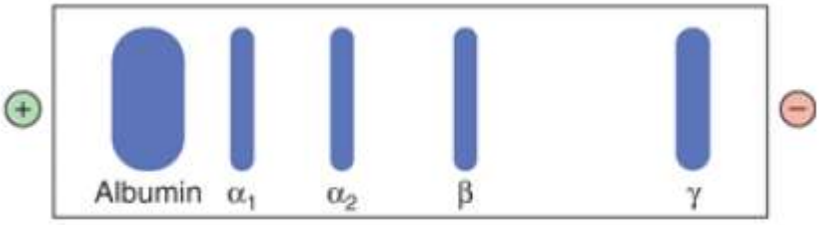


These are gels containing bands ,the largest band is the albumin because it is a main part and the other bands are approximately the same but γ band is somehow larger than the others (α1 , α2, β)

- If we bring the gel and put in a **densitometer** we measure the density found in the gel then we divide them and find that the albumin has the largest percentage (about 60% of the whole sample) then the rest of the percentage is distributed between (α1 , α2, β, γ)

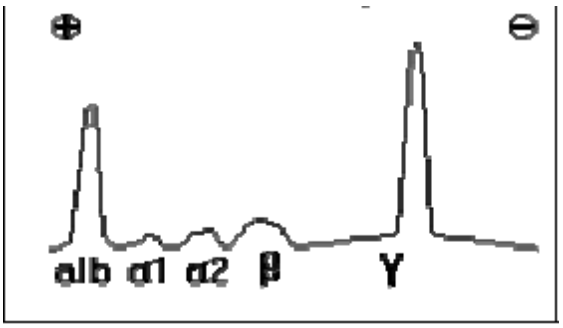
  **This is how the interpretation of plasma proteins occurs , this is important in diagnosing some diseases ;if this percentages differ (increasing γ very much or increasing or decreasing albumin very much).

  NOTE: *Where are the proteins produced?
  In the liver (proteins go to the blood then they become produced in the liver, so if we have any problem in the liver there will be a decrease in protein percentages except γ since they are produced by plasma cells)

  *Where are the immunoglobulins (antibodies) produced?
  In the plasma cells that come from lymphocytes ((lymphocytes are found in lymph nodes,spleen ,thymus)

  - Plasma cell myeloma(cancer in the plasma cells), plasma cells start to multiply in large amounts &there is an increase in the antibodies

EXAM QUESTION: what is this case??
*plasma cell myeloma



Increase in γ globulins rate so it become close to the albumin indicates cancer while increase in small amount indicates inflammation and numerous antibodies.

Refer to slide #9

-Longstanding inflammation is a general case
-plasma cell myeloma :note that the γ rate is too high
-chronic liver failure :percentages of proteins are too low but the rate of γ globulins is not affected & it may increase relatively because its production is not in the liver .

NOTE:the differentiation of diseases in this slide is not required but you have to know that it has an interpretation related to our life.

REMEMBER :electrophoresis on any serum sample gives albumin which is negatively charged and smaller than other proteins so it will be the fastest in transportation.

Refer to slide #8
Globulins are divided into 3 bands :

- α band:
- α1 region consists mostly of **α1-antitrypsin** (this protein is related to emphysema ,smoking ,phenotype that affects some populations)

- α2 region is mostly haptoglobin (it binds free hemoglobin in the blood), α2-macroglobulin, & ceruloplasmin (it binds the copper in the blood)
- β band: transferring (it is related to hemoglobin and iron transport through the blood), LDL, complement system proteins (we will only explain β2 macroglobin)
- γ band: the immuno-globulins

Refer to slide #10
*Synthesis of plasma proteins occur mainly in the liver
*γ-globulins (immunoglobulins)are produced in plasma cells that is found in the lymph nodes, bone marrow, spleen)
*most of the plasma proteins are synthesized in the liver as preproteins(inactive form) then they become active

- Why are proteins produced in the inactive form?
  1)because we want it in a specific destination not the destination it is being produced in &through its way to the required destination it is broken down to become active
  2)because we don't want it to work unless it is needed

  EXPLANATION:the liver produces around 12 grams/day albumin(1/4 of the production of the liver of proteins is albumin) it is produced within the liver cells so it has to be transported to the plasma, firtsly it goes out from the liver cells .When proteins are synthesized , signal peptides are produced with them to take the proteins to their destinations, so this signal peptide can attach to the membrane and then exit the protein out of the cell then it undergoes further breaking down to be in the active form during its way to the plasma.

- Plasma proteins generally undergo multiple posttranslational modifications such as :
  -proteolysis:breaking down of some parts to be in the required form
  -glycosylation:adding carbohydrates
  -phosphorylation

  REMEMBER:most of the plasma proteins are glycoproteins except albumin

- **Transit times:**
  Transit time of the plasma proteins from the liver to the plasma is different among different proteins (30 min to several hours)

- Glycoproteins are either N- or O- linked
  *What do we mean by saying N- or O- linked ?

When carbohydrates attach to proteins they either attach to N(N- linked ,asparagines) or O(O-linked, serine ,threonine ,sometimes tyrosine)

REMMBER: albumin is not glycosylated
EXAM QUESTION:choose the wrong statement:
Albumin is attached to carbohydrates

Refer to slide #11
*Most of the plasma proteins have something called polymorphism

*What is polymorphism?
EXPLANATION :Proteins are sometimes mutated ,this mutation is transferred from one generation to another without causing a disease instead ,causing a change in protein's shape without affecting its function or changing the function to some extent or changing the characteristics without affecting the function or changing the capacity of the protein, so if this mutation was transferred from one generation to another and its percentage in the society is more than 1% then it is called polymorphism

*example on polymorphism:
ABO blood grouping
-most common blood type is : O
(The blood types A , B, AB are not a mutation or disease but they are polymorphisms)

*examples of proteins that have polymorphism: α1-antitrypsin, haptoglobin, transferrin, ceruloplasmin, and immunoglobulins

- Separation of plasma proteins:
  1) electrophoresis:separates the proteins with different amino acid composition,we put a gel in a very thin way and give it longer time,at the end different polymorphic proteins will be separated

  2)isoelectric focusing:changing the amino acids will change the total charge present on the protein,so through this technique you can also separate plasma proteins from each other

❖ **HALF LIVES**

-half lives of plasma proteins are very different
-albumin's half life is 20 days while haptoglobin's is 5 days

EXAM QUESTION:choose the wrong statement:
The half life of albumin is 5 days

❖ How can we know the half lives of the proteins?
By labeling the protein with a radioactive substance such as Iodine then you let it circulate through the blood then by reaching half of its concentration you will know the half life.

❖ Diseases affecting half lives:
❖ What accelerates degradation of a protein?
1)renal diseases: in this case the kidney cannot undergo reabsorption so the substances will get out through urine & it loses its plasma proteins& the half life decreases

2)chronic inflammation in the intestines: the inflamed area is red because of more blood supply coming towards this area(the plasma can get out of the blood vessels to reach the tissue) increasing plasma proteins getting out from the blood outside to the intestines then it is lost from the body through faeces so the half life will decrease. (Chrohn's disease)
Protein losing gastroenteropathy (gastric problems that cause protein loss)

"A DAY WITHOUT LAUGHTER IS A DAY WASTED "---CHARLIE CHAPLIN

I am sorry for any mistake ☺ 

Good luck ☺