Lecture one

♡ Biochemistry

chemistry inside living cells.

(structure and function of macromolecules)

All macromolecules end up as acetyl coA

☆ Acetyl CoA ⟫ Krebs cycle → oxidative phosphorylation→ ATP.

♡ all macromolecules produce energy (but not the same amount) (fat > sugar)

♡ Haematocrit OR Packed cell volume :

The haematocrit blood test determines ?

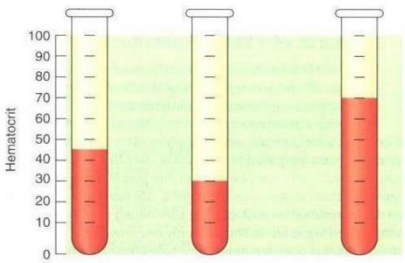
the percentage of blood cells in a given sample.

** RBCs the majority **

in males =47% ,

females it = 42%.

😉Any change (increase or decrease) = disease

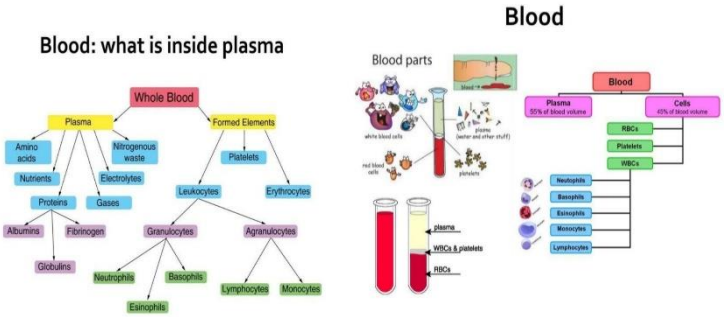


♡ Blood is made of 2 components: (everything)

the main way of communication between organs and the outside environment.

1. Plasma (liquid that cells are suspended (not soluble
2. Cellular component (RBCs (erythrocytes), WBCs (leukocytes) and Platelets)

the mixture of WBCs and platelets "Buffy Coat"



➢ Composition: ▪ Water (92%) ▪ Solids (8%)

➢ More than 500 plasma proteins have been identified

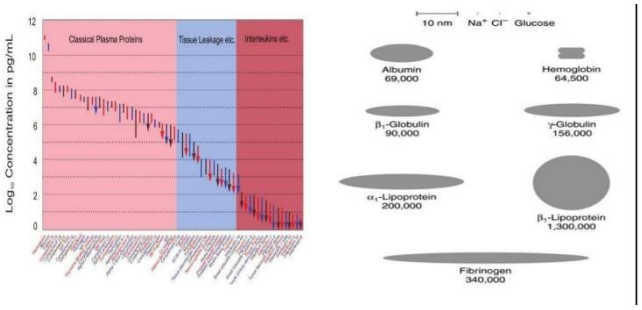
➢ Normal range 6-8 g/dl (the major of the solids)

➢ Simple & conjugated proteins (glycoproteins & lipoproteins)

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^-,$HCO3^-$,$HPO4^{2-}$, $SO4^{2-}$

♡ Proteins differ in MW and their shape



♡ Separation of plasma proteins (2 techniques):

1. Salting out :

☆(ammonium sulfate)☆

Plasma ✔

the precipitation of proteins depending on their solubility

The lower the solubility of a protein, the earlier it will precipitate (salts > proteins)

♤ fibrinogen, albumin, and globulins

2. Gel electrophoresis:

☆(most common)☆

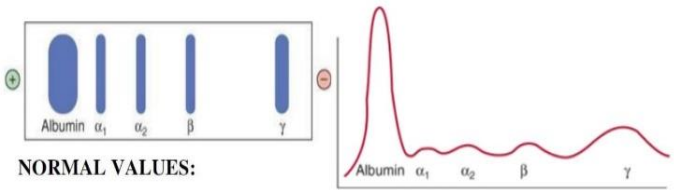
Plasma ✘

Serum ✔

(serum; Plasma without clotting factors (mainly fibrinogen)) (defebinated plasma)

Mechanisms :

The serum added to the wells and the plasma proteins (negative charge , MW) will result in 5 bands including : albumin, alpha1, alpha2,beta gamma



NORMAL VALUES:

Name	Absolute values (g/l)	Relative values (%)
Albumins	35 – 55	50 – 60
α1-globulins	2 – 4	4.2 – 7.2
α2-globulins	5 – 9	6.8 – 12
β-globulins	6 – 11	9.3 – 15
γ-globulins	7 – 17	13 – 23

➢ Albumin is smaller than globulin, and slightly negatively charged (one band only)

Albumin makes (50% to 60%) of the 6-8 grams plasma proteins which means it is approximately (3.5-5.5 g/dl).

➢ Globulins (3 bands):

➢ α band: a1 MW = a2 MW

✓ 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 (5 types = Ig (MAGDE), B cell

Salting out ammonium sulfate	the precipitation of proteins depending on their solubility	fibrinogen, albumin, and globulins	Plasma ✔
Gel electrophoresis most common	The serum added to the wells and the plasma proteins (negative charge , MW)	albumin, alpha1, alpha2,beta gamma	Plasma ✘ Serum ✔

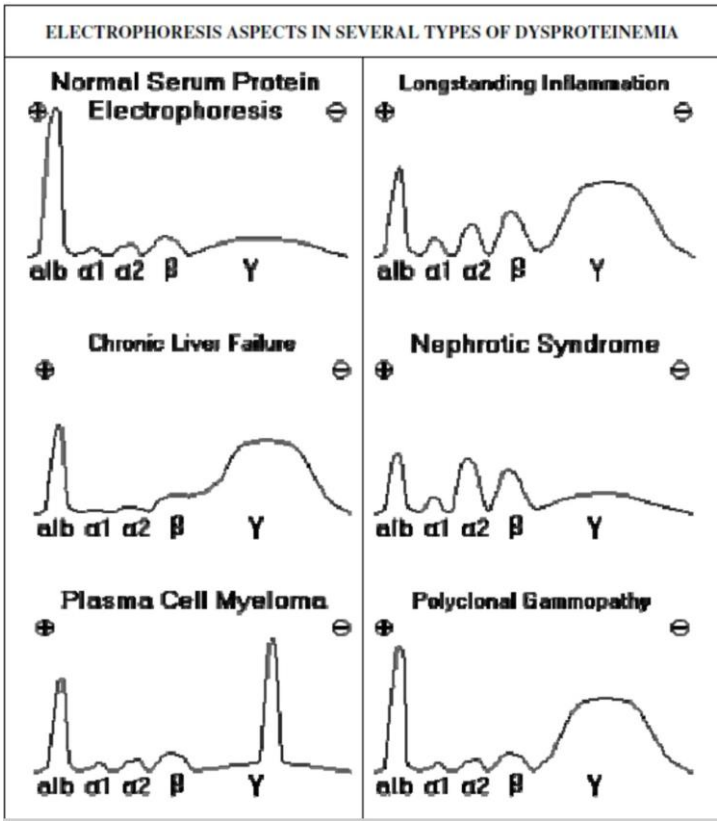
alpha band separated easily, and if we give more time, beta band will separated too.☐

** Densitometer measures the thickness of the band and convert it to a curve. 5)

** Concentrations ; albumin > Gamma > alphas and the beta :)

♡ DISEASE

Longstanding inflammation	globulins concentration increases
Renal failure (filtration failure or nephrotic syndrome)	some proteins were lost from the blood (in urine) ✸not selective to any specific type of protein.
Liver failure (alcoholic liver, cirrhosis, fibroses hepatitis)	all proteins except gamma globulins their percentages will come down.
plasma cells with Cancer (mature B lymphocytes)	gamma globulins will rise ♥One type of gamma rise ♥ 5 types of gamma rise



Most of the plasma proteins are made inactive (preproproteins) and they are modified later, this is done for 2 reasons:

1,no need for the protein to function unless its needed (it will be activated later as in fibrinogen).

2.,if the site of synthesis differs from the site of function.

✔ 30 mins up to several hours

** All plasma proteins are glycosylated except for albumin(carbohydrates are important to improve solubility, communication and attachment). becomes denser (viscosity increases) and harder to move.

♡ 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 because the concentration of albumin is the highest, and attachment of the carbohydrates increase the solubility and that lead to increases viscosity.

♡ Plasma protein and polymorphism

☆ mutation is a permanent alteration in at least one nucleotide in the DNA, it might result in a change of one or more amino acids

• Not all mutations result in diseases.

☆ POLYMORPHISM : When a mutation affects 1% or more of the population

** any mutation may result in a different sequence of amino acids, thus different shapes of a protein.

SINGLE-NUCLEOTIDE POLYMORPHISM (SNPs): change happens in one nucleotide

Almost all plasma proteins have polymorphisms (not all people have the same sequence of amino acids for plasma proteins)

➢ A mendelian or monogenic trait

➢ Exists in population in at least two phenotypes, neither is rare

➢ The ABO blood groups are the best-known examples

➢ α1-antitrypsin, haptoglobin, transferrin, ceruloplasmin, and immunoglobulins

➢ Electrophoresis or isoelectric focusing

♡ Plasma protein half-lives

• Plasma proteins vary in half-lives (albumin 20 days, haptoglobin only 5 days)

Proteins' half-lives are determined through a procedure known as isotopic labeling

• Half-lives of plasma proteins are affected by diseases, mostly GI diseases because GI has a high blood supply

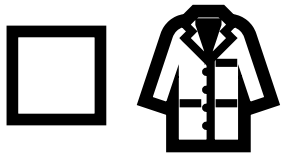
➢ Determined through isotope labeling studies (I131)

➢ Albumin & haptoglobin (20 & 5 days)

➢ Diseases can affect half-lives (ex. Crohn's disease), albumin may be reduced (1 day)

➢ Protein-losing gastroenteropathy (gastro: stomach, entero: intestines, pathy: disease)

" Protein-losing gastro enteropathy "



DOCTOR

Functions of plasma proteins:

Functions of plasma proteins:

Specific functions (vary from one protein to another)

1)Enzymes (e.g. rennin, coagulation factors, lipases)

2)Humoral immunity (immunoglobulins)

3)Blood coagulation factors

4)Hormonal (Erythropoietin)

5)Transport proteins (Transferrin, Thyroxin binding globulin, Apolipoprotein)

General functions (for all plasma proteins due to their common amino acid structures)

1) A nutritive role: when there is no food these proteins are broken down to provide energy.

2) Maintenance of blood pH (amphoteric property): all act as a buffer (H+ donor and acceptor) regardless to its nature because the existence of free carboxylic and amide groups at the terminus.

3) Contribution to blood viscosity: anything dissolve in water increases the viscosity.

4) Maintenance of blood osmotic pressure (oncotic pressure): it is the force applied by proteins themselves within blood on the plasma (water) to keep water inside the vessels (attract water), so it won't let water leak outside the vessels into the interstitial fluid.

Starling forces

✓ Arterioles, venules vs. tissue hydrostatic pressure (37 & 17 vs. 1 mmHg)

✓ Plasma proteins oncotic pressure is 25 mm Hg

✓ Edema can be a result of protein deficiency

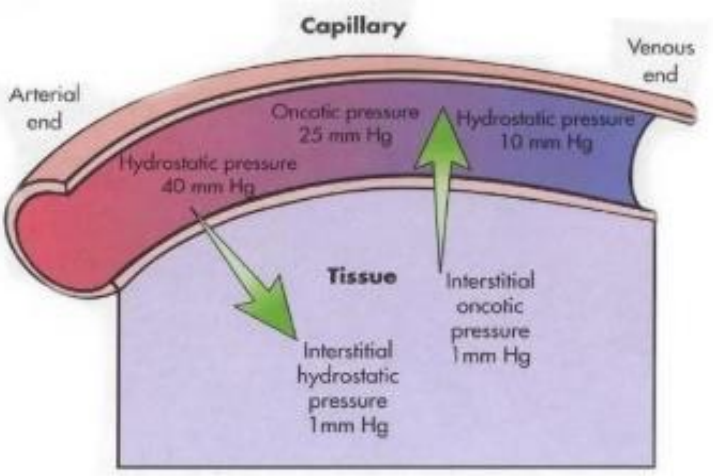
** Starling forces: two opposite forces controlling the exchange of nutrients between capillaries and tissues.

1) Oncotic pressure (directs water to the vessels).

2) Hydrostatic blood pressure: pressure applied by the fluid in the wall of vascular system. (to the interstitial fluid).

○ NORMALLY proteins control the process and don't allow water to get outside the vessel

	Arteriole	Venule
Blood pressure (mm Hg)	40	10
Osmotic pressure (fixed)	25	25
Resultant	15 outside with nutrients	15 inside with wastes



** In abnormal conditions (heart failure or kidney problems) it is not balanced

	Arteriole	Venule
Blood pressure (mm Hg)	40	10
Osmotic pressure(fixed)	20	20
Resultant	20 outside with nutrients	10 inside with wastes

Acute-phase proteins

➢ Levels increase (0.5-1000 folds), acute inflammation, tissue damage, chronic inflammation & cancer. C-reactive protein (CRP), α1 -antitrypsin, haptoglobin, & fibrinogen

➢ Interleukin-1 (IL-1), main stimulator (gene transcription)

➢ Nuclear factor kappa-B (NFkB): Exist in an inactive form in cytosol, activated and translocated to nucleus (interleukin-1)

➢ Negative acute phase proteins: prealbumin, albumin, transferrin

A lot of plasma proteins are called ACUTE-PHASE PROTEINS, because under cases of acute inflammation, tissue damage, cancer or chronic inflammation, some proteins' concentrations increase dramatically (sometimes 1000-fold of their regular concentration)

THE MECHANISM:

1. Inflammatory processes
2. Activate Interleukin-1 (IL-1) targets liver cells
3. translocation to a transcription factor* called Nuclear factor kappa B (NFkB) from the cytosol (inactive form) to the nucleus (active form).
4. In the nucleus (NFkB) binds to the DNA
5. start transcription (mRNA)
6. then translation to produce proteins (increasing their concentration)

For example

C-reactive protein (CRP)

α1 -antitrypsin

haptoglobin

fibrinogen

Negative acute-phase proteins

Some proteins decrease in concentration (or do not get affected at all) in cases of acute inflammations, chronic inflammations or cancer

Prealbumin, albumin, transferrin

Past papers ✔

1-Which of the following statements regarding blood composition is FALSE:

A) Blood of a patient with anemia is expected to contain more than 55% plasma.

B) Fibrinogen is present in plasma while absent in serum

C) The blood cells that makes up the most of hematocrit are: Red Blood Cells

D) The most abundant plasma protein is synthesized in the liver

E) None of the above is false

2 -What is the most abundant plasma protein in normal individuals?

A)alpha1-antitrypsin

B)haptoglobin

C)albumin

D)gamma globulin

E)fibronogen

3-Which major class of plasma proteins is not synthesized in the liver?

A) alpha1-antitrypsin

B)haptoglobin

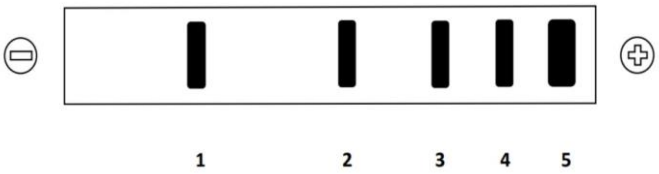
C)albumin

D)gamma globulin

E)fibronogen

4 -Gel electrophoresis was applied to a serum sample, and the resulting 5 bands (representing albumin, γ, β, α1, α2 globulins) are shown in the adjacent figure. Which of the bands represents albumin:

A) Band 1



B) Band 2

C) Band 3

D) Band 4

E) Band 5

1)What cells we can find in the blood (cellular component)?

a. RBCS, WBCS, epithelial cells

b.RBCS, WBCS, platelets

c. Osteoblast, osteoclast, osteocytes

d.Microglial cells, Kupffer cells, mesangial cells

2) Plasma components:

a. Amino acids, LDL, nitrogenous waste, electrolytes,

gases, proteins

b.Amino acids, lipids, nitrogenous waste, bile

pigments, gases, proteins

c. Amino acids, gases, electrolytes, nutrients,

nitrogenous waste, proteins

d. All of the above

3) Choose the correct statement;

a. The shape of the protein determines the function

b.The shape of the protein determines where the protein was synthesized

c. The shape of the protein effects the structure

d.None of the above

4) What is the most common way to purify plasma proteins?

a. Gel electrophoresis
b. Western blotting
c. Immunotherapy
d. .Salting out

5) best known example for polymorphism?

a. ABO blood type

b. Anaemia

c. Cancer

d. More than one of the above

6) A 66 years old woman was admitted to the hospital with severe pain in her abdomen when she was examined the doctors observed severe anaemia and pitting oedema on the effected part of her body and the laboratory results indicate a dramatic decrease in hemoglobin and haptoglobin concentration and it was mentioned that the pain was due chronic blood loss and a chronic disease. What is wrong with the woman?

a. Protein losing gastroenteropathy

b. Alcoholic liver

c. Nephrotic syndrome

d. Fibrosis hepatitis

7) Albumin percentage relative to plasma proteins

a. 50%-60%

b. 10% - 20%

c. 90% -95%

d. None of the above

8) what is the effect of liver failure on the percentage of all proteins

a. Decrease all proteins percentage except immuno-globulins

b. Gamma globulins are not affected

c. The band thickness of all proteins in electrophoresis will decrease

e. a + b

9) If albumin was glycosylated what will happen?

f. a. Increase the viscosity of the blood and it becomes
g. harder to move
h. b. Increase solubility of albumin in the blood
i. c. Other plasma proteins concentration will decrease
j. d. More than one of the above

10) Describe interleukin 1:

a. A gene modifier

b. Signaling molecule

c. Can be considered part of cytokines

d. b + c

Lecture one	
Read past papers	✔
Sheet 1 read 5 times	✔
Sheet 1 notes Main ideas	✔
Write word notes	✔
Anki to save	✔
Mind map	✔
Review	/
Past papers explaining	✔
Vedio	

lecture one

metabolism

salma Alshiekh

Plasma

Plasma proteins

➢ More than 500
6-8 g/dl of solids
➢ Simple & conjugated proteins

Synthesis

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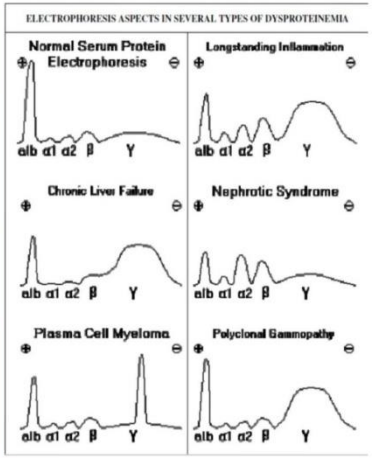

Disease

Notes ✓💜

* One of blood contains

*liquid that cells are suspended (not soluble)

* the main way of communication between organs and the outside environment.

Separation

Subtopic

Gel electrophoresis

Salting out ammonium sulfate	the precipitation of proteins depending on their solubility	fibrinogen, albumin, and globulins	Plasma ✔
Gel electrophoresis most common	The serum added to the wells and the plasma proteins (negative charge , MW)	albumin, alpha1, alpha2,beta gamma	Plasma ✘ Serum ✔

polymorphism

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- Maintenance of blood pH (amphoteric property)
- Contributes to blood viscosity
- Maintenance of blood osmotic pressure

Specific functions

- Enzymes (e.g. rennin, coagulation factors, lipases)
- Humoral immunity (immunoglobulins)
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- Hormonal (Erythropoietin)
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Functions