In the previous lecture we have started talking about plasma protein (concept, classification ...)

In this lecture we will continue talking about them, and talking briefly about albumin.

**Plasma proteins half-life**

- The time that needed to reach the half of the concentration of a protein.
- Determined through isotope labeling studies (I131)

  We label a protein with the (I131), then introduce it into circulation keep watching it until it reaches the half concentration of the original concentration then determined the half-life.

- Plasma proteins vary in their half-lives Albumin & haptoglobin (20 & 5 days)
- Diseases can affect half-lives (ex. Crohn’s disease), albumin may be reduced (1 day)
- Protein-losing gastroenteropathy is characterized by the loss of plasma proteins into the GI tract.
Functions of the plasma protein

1- **General functions**: mean all plasma proteins do them because they share common features:

* They are built from amino acids
* They are found in the blood especially in the plasma

**Note: any function for any plasma protein that is a result from its unique structure (side chains of its amino acids, arrangement of its amino acids ......) Isn’t considered general function for all plasma protein.

a) **A nutritive role**: all plasma proteins can be broken down to give energy (metabolism of plasma proteins) absolutely in the absence of fats and carbohydrates.

b) **Maintenance of blood pH (amphoteric property)**: working as buffering agents.

Because all proteins have a free carboxyl group and free amine group which can accept or donate protons.

c) **Contributes to blood viscosity**: all plasma proteins are glycoproteins (attached to carbohydrates) except for albumin.

Attaching carbohydrates to plasma proteins will increase the negative charges so water molecules attach strongly to plasma proteins in order to increase viscosity.
Albumin already has higher negatively charge (so glycosylation isn’t necessary for it).

d) **Maintenance of blood osmotic pressure**: is a result of dissolved solids in the blood mainly plasma proteins and always in the opposite direction of hydrostatic pressure

2- **Special functions**: for a certain plasma proteins.
   a) Enzymes (e.g. rennin, coagulation factors, lipases)
   b) Humeral immunity (immunoglobulins)
   c) Blood coagulation factors
   d) Hormonal (Erythropoietin)
   e) Transport proteins (Transferrin, Thyroxin binding globulin, Apolipoprotein).

**Starling forces**

**Normal blood pressure (120/80)** **extra info**

Blood is liquid so it has pressure on the walls of blood vessels (**hydrostatic pressure**). This pressure is trying to get water outside the capillaries into interstitial fluid in a process called **Filtration**.

Another type of pressure is found due to presence of plasma proteins called osmotic pressure. This pressure is trying to get water inside (**reabsorption**).

In the arterial side of capillaries: hydrostatic pressure is higher than oncotic pressure (filtration will occur)

In the venous side: oncotic pressure is higher than hydrostatic pressure (reabsorption will occur)
in normal conditions the net movement of water is zero.
(Filtration in arterial side is equal to reabsorption in venous side).
**Assume you have a pathogenic reason leads to reduce concentration of plasma proteins.

\[
\text{Oncotic pressure} \quad \downarrow \quad \text{reabsorption} \quad \downarrow
\]

Accumulation of water in interstitial fluid will occur (edema).

In case of liver failure: plasma proteins will decrease so the oncotic pressure will decrease. Suppose the oncotic pressure 20 mmHg instead of 25 we will get this results:

**In arterial end**
40-20 = 20 (20 filtration)

**In Venous end**
10-20 = -10 (10 reabsorption)

More filtration than reabsorption this causes Edema.

**Acute phase proteins**

(الدكتور ركز هاد الموضوع سؤاله اكيد في الامتحان)

In the case of acute infection, chronic infection, cancer inflammatory process start to release inflammatory mediators (markers, signals)
Such as:
interleukin -1 (exported by certain cells and binds to liver cells)

**In the cytosol of liver cells, there is a transcription factor called nuclear factor kappa-B (NFkB.) (In the inactive form).

When the interleukin-1 binds to the liver cells, (NFkB) will be activated and Translocate to the nucleus.

It will bind to the certain promoters on DNA that activate producing mRNA which translated into several types of proteins (acute phase proteins).

1) C-reactive protein
2) α1 –antitrypsin
3) haptoglobin
4) Fibrinogen.

**Others plasma proteins won’t change or may reduce in concentration (Negative acute phase proteins).

1) Albumin
2) prealbumin
3) transferrin.

**Albumin**

The main transporter in the blood

(مترو الانفاق)

1) The Major Protein in Human Plasma, 69 kDa, half-life (20 days)
2) The main contributor to the osmotic pressure (75-80%) (the highest concentration)
3) Synthesized as a preproprotein in the liver, then some modification to reach the final shape.

4) Liver: 12 g/day (25% of total protein synthesis)
   We can use the concentration of albumin in the liver test.
5) One polypeptide chain, 585 amino acids, 17 disulfide bonds (so its final shape is fixed).
6) Proteases subdivide albumin into 3 domains each domain has a certain function.
   One of those domains is called **drug binding domain or albumin binding domain**.
7) Ellipsoidal shape (viscosity).
8) Anionic at pH 7.4 with 20 negative charges.

**binds various ligands:**

1) Free fatty acids (FFA)
2) Certain steroid hormones
3) Plasma tryptophan
   Remember tryptophan is non polar (so it needs transport proteins in the blood).
4) Metals: Calcium, copper and heavy metals.
5) Bilirubin: all structures in our bodies must undergo metabolism process such as: heme group (in the liver), then it is converted into bilirubin in a certain pathway.
*Bilirubin accumulates in the liver then transfer to (Gallbladder).
*In some liver diseases, bilirubin goes to the blood, then to the tissues. (Hepatitis A).

6) Drugs: sulfonamides, penicillin G, dicumarol, aspirin on the binding domain of albumin.

**Drug-drug interaction**

*Note:* Albumin is the site of bind many drugs so we may find more than one drug that bind to the same site on albumin.
*The drug with the higher concentration and higher affinity will bind.
*The free drug affects the body (not the binding one)

**Bilirubin-Aspirin interaction**

Children and newborns cannot take aspirin because it binds on albumin instead of bilirubin.
Accumulation of bilirubin will occur in brain
Leads to mental retardation (kernicterus) Bilirubin toxicity.

**Phenytoin-dicoumarol interaction**

Phenytoin is a treatment for Epilepsy. Dicoumarol is anticoagulant substance. Both are competitive ligands
And you shouldn’t take them in the same time.

**Analbuminemia (no albumin)**

1) There are human cases of analbuminemia (rare)
2) Autosomal recessive inheritance.
3) One of the causes: a mutation that affects splicing
4) Patients show moderate edema!!

**Note**: because the albumin is the highest concentration in the plasma, so hypoalbuminemia means hypoproteinemia.

**In the case of analbuminemia**: we predict that severe edema will occur??

But in the real situations, moderate edema has occurred because the liver makes compensation by producing another plasma proteins to keep the general function of plasma proteins (Maintenance of oncotic pressure).

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**Hypoalbuminemia**

Edema seen in conditions where albumin level in blood is less than 2 g/dl

1) Malnutrition (generalized edema)
2) Nephrotic syndrome
3) Cirrhosis (mainly ascites)
4) Gastrointestinal loss (Protein-losing gastroenteropathy) reducing the half-life of albumin.
Hyperalbuminemia

Dehydration (relative increase) not actual increase because the concentration of plasma proteins is constant, but water can decrease so plasma proteins can relatively increase.