2

Biochemistry 2

Doctor 2018 | Medicine | JU

Sheet

Slides

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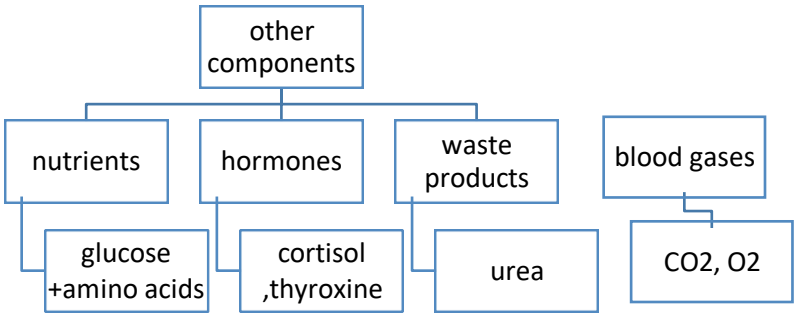
Components of Plasma

Note : this sheet had been corrected and we have added one more page

1- **Water 90%**
2- **Plasma proteins 6-8%**

3- **Electrolytes (Na and cl) 1%**

4- **Other components such as:**



Plasma proteins A complex mixture that includes hundreds of proteins

- **Albumin - Globulins - Fibrinogen**

**** Plasma proteins differ in shapes and sizes**

Important note:

Albumin is the smallest and most abundant protein.

Half-life of plasma proteins

- **to measure the half- life of plasma proteins:**
  1) **First we must isolate the protein**
  2) **Labeling with radioactive iodine I-131**
  3) **Reinject the sample to the patient**
  4) **Follow the change over time.**

- **During degradation of a protein, the radioactive signal fades out over time so we take blood samples regularly until we observe that the radioactive signal is one half of the peak value.**

Half-life of plasma protein: is the time for radioactivity to decline from its peak value to one half of its peak value .

NOTE: Degradation of a certain protein does not mean that it will become close to zero. Because for example albumin, when albumin is in degradation there are also some albumin are being synthesized (Turnover rate).

13:00

- **Most plasma proteins are synthesized by hepatocytes in the liver, except:**
    - **Y-globulins (synthesized by lymphocytes)**
    - **A clotting factor called Von -Willebrand factor (synthesized in vascular endothelium)**
- **Most plasma proteins get modified (glycosylation) which is addition of sugar, thus they are Glycoproteins , except:**
    - **Albumin, which is classified as a simple protein (no modifications or extra (prosthetic) groups**
- **Glycosylation can be N-linked or O- linked :**
    - **N-linked is on the asparagine amino acid and it happens in the Rough ER then to the Golgi**
    - **O-linked on serine or threonine and it happens in Golgi**

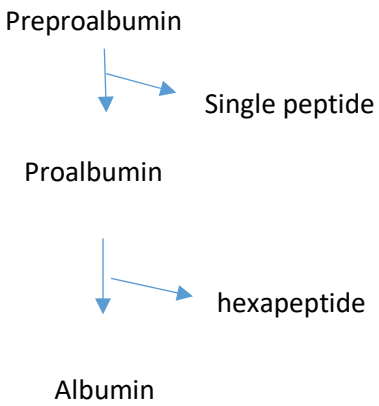
    - **After modification of the proteins. The termination signal sequence (N-terminus) gives the signal to the cell to package the protein in vesicles through the secretory pathway to secrete the proteins to the blood stream.**
    - **That's why genes for plasma proteins code for an amino terminal signal sequence**

NOTE: All plasma proteins are found in serum except for Fibrinogen.
- **After coagulation the fibrinogen in plasma is converted to fibrin**
- **After coagulation plasma becomes serum.**

Albumin

- **60% of plasma proteins are Albumin**
- **Albumin levels varies with age = 3.4 – 4.7 g/100ml**
- **25% of total protein synthesis by liver = one half of the secreted protiens**
- **69 kDa**
- **One polypeptides with 585 amino acids**
- **Half-life 20 days**
- **12 grams of albumin are produced daily from the liver**

Albumin synthesis

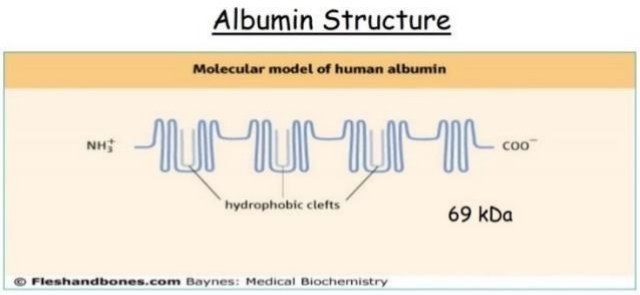


- **The difference of Preproalbumin is when you remove a single peptide and secrete it becomes Proalbumin**

- **Proalbumin is a fast indicator for many diseases because it gives**
  Quick Information in cases of changes in liver function. Why?
  Because its half life is shorter than albumin (2 days).

Example.. If a patients liver is damaged, you cant diagnose him by albumin levels because you will need 20 days to detect changes in albumin levels, but Proalbumin decrease will be detected in about 2 days only! Thus making it very practical

Albumin structure



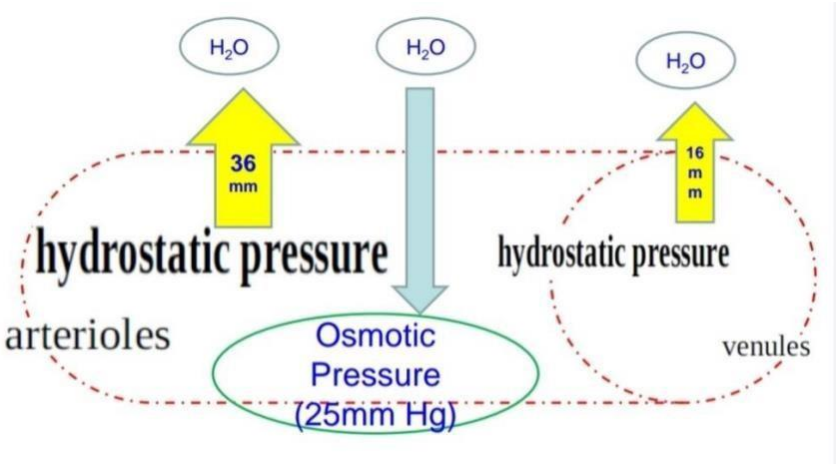
- Ellipsoidal shape
- It is highly polar but contains three hydrophobic clefts which acts like pockets and covers hydrophobic amino acids.
- Mainly negatively charged in physiological ph. (7.4) with 20 negative charges.

• Ellipsoidal shape

Plasma proteins help determine the distribution of fluid between Blood and tissues

- The hydrostatic pressure is the pressure that is exerted by water (in plasma) to the walls of blood vessels thus pushing water out of the vessel.
- While the osmotic pressure pushes water in to the blood vessels.

Have a look at the following diagram



-If You look carefully you will see that in the arterioles the hydrostatic pressure is 36 mmHg (out of the vessel) while the osmotic pressure 25mmHg (into the vessel) thus making the net pressure 11 mmHg (out of the vessel)

- But in venules the hydrostatic pressure and osmotic pressure are (16 and 25 respectively) thus making the net pressure 9 mmHg into the vessel.

Colloid osmotic Pressure is the osmotic pressure exerted by protein (without moving proteins)

- **Albumin is responsible for 80% of the colloidal pressure**
- **At normal albumin concentration, water movement in and out of the vessels will be balanced due to normal colloid pressure.**
- **While as if concentration of albumin is low (hepatitis , cirrhosis, fibrosis , liver damage and renal failure) , the colloid pressure will decrease thus making water flow out of the vessel will increase = thus making edema(swelling).**
- **Albumin must not be excreted by the kidneys in normal cases.**
- **So if there is renal failure there will be high amount of protein in the urine thus making low albumin conc.**

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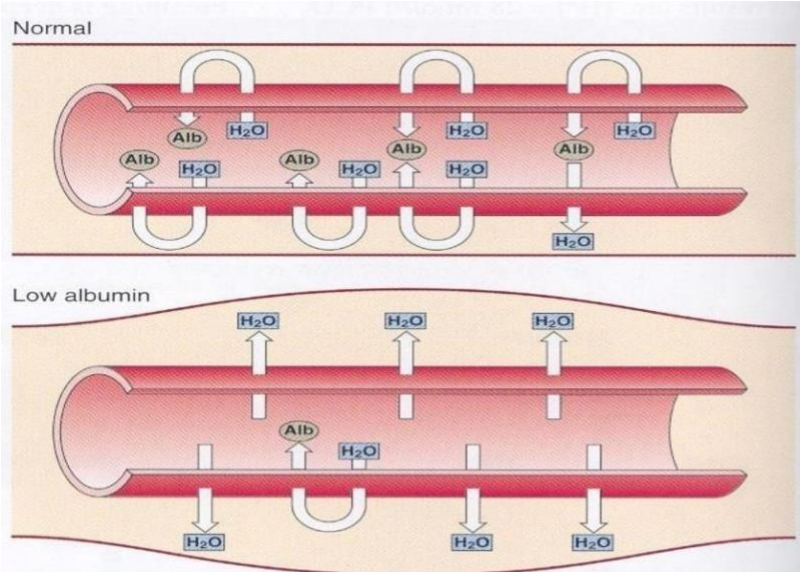


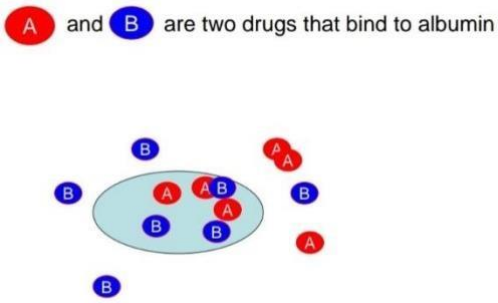
Albumin binds to a variety of substances such as :

- **Bilirubin(a metabolite of heme group)**
- **Free fatty acids (In keto diets the primary source of energy are lipids thus the body breaks triacylglycerol into fatty acids and then albumin carries hose fatty acids in the bloodstream because they are hydrophobic)**
- **Some steroid hormones (hydrophobic)**
- **Some drugs like salicylic acid (aspirin) and sulfonamide**
- **Ca2+**
- **Cu+**

Binding of drugs to albumin can result in drug-drug interaction such as:

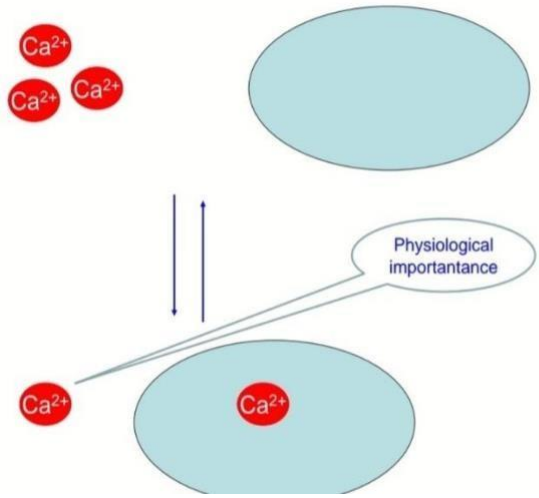
1- **If a patient takes two drugs (A and B) and they both are carried by albumin The two drugs in this case will both have a stronger effect the their normal effect. Why?**
Because for example the patient took the drug A. Some of the drug A in the blood will be bound to albumin while the others will be free (the free

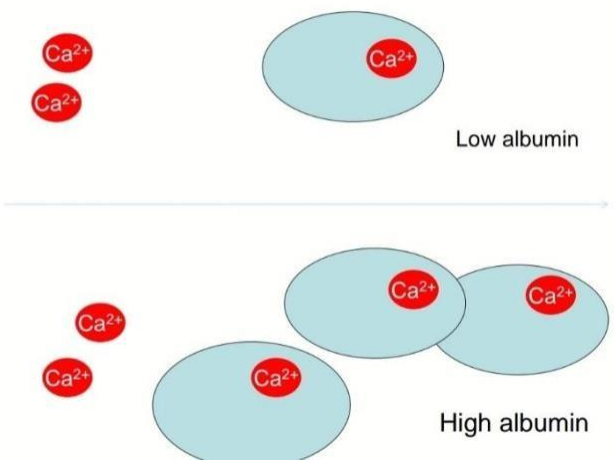
drug molecules are the effective molecules because the albumin-bound drug molecules cannot leave albumin and bind to the intended target)
So when the patient also takes drug B it will compete with drug A in binding with albumin and take some of the albumin for it self thus making more free drug A molecules and vise versa.



2- Calcium ions:

- **Calcium is important for blood clotting**
- **Calcium can also bind to albumin**
- **The physiologically important calcium ions are also the ones that are free in the blood (not bound to albumin)**
- **In blood tests the amount of calcium detected is in fact both the free and the albumin bound calcium.**
- **Sometimes the albumin level In the patient is higher thannormal In this case the amount of total calcium will increase to maintain the same number of free calcium ions**
- **And that's why when we want to test calcium levels we must test also albumin levels**





Decreased concentration of albumin causes:

-**Inadequate source of amino acids (malnutrition and muscle wasting)**

-**Liver disease (Total protein can be normal but albumin will be decreased when liver is damaged)**

-**Gastrointestinal loss (leakage of fluid from inflamed or diseased mucosa.. for example when a blood vessel leaks due to diseased mucosa, the concentration. Of albumin will be relatively higher and that will act as a signal to decrease the rate of producing albumin)**

-**Renal disease**

(penetration of albumin through glomerulus)

Analbuminemia

-A very rare genetic disease
-Defect in the processing of mRNA of albumin
-The mode of inheritance is Autosomal recessive inheritance

Which means that you need to have two copies of abnormal gene to be diseased

-Makes moderate edema (it is not severe because of the higher conc. Of other proteins to compensate the albumin loss)
-Which means that when the body has Analbuminemia it synthesizes

Causes of decreased plasma albumin:

I. Decreased synthesis
   A. malnutrtion
   B. malabsorption
   C. advanced chronic liver disease

II. Abnormal distribution or dilution
   A. overhydration
   B. increased capillary permeability like in septicemia

III. Abnormal excretion or degradation
   A. nephrotic syndrome
   B. burns
   C. hemorrhage
   D. certain catabolic states
   E. loss of protein from the digestive tract

IV. Rare congenital defects
   A. hypoalbuminemia
   B. analbuminemia

Prealbumin : its an early indicator of problems in albumin especially that its half life is short (2 days)
So any problems in the liver or any tissue necrosis that affects the synthesis of albumin will be reflected on the prealbumin , it moves ahead of albumin since its smaller in size
- it combines with and transports thyroxine hormone (two forms T3/T4)
T3 is the active form
It also binds to Retinol binding protein (vitamin 2)

Acute phase proteins :

In some cases the levels of protein could be highly affected (especially plasma proteins)
They can increase 1000 times , maybe only 50 times < it depends on the situation

Such thing happens in :
Cancer
Chronic inflammatory states
What happens in such cases is : the expression of some protein increases such as(C reactive proteins) and alpha-1 antitrypsin and haptoglobin

C reactive protein :

Is a protein that is undetectable (we cant measure it in a healthy person) it only appears in inflammatory diseases such as :
Acute rheumatic fever
Some bacterial infections
Tissue damages
All of these express an increase in c reactive proteins

This protein is going to interact with a substance called (c-substance) that's why its called c reactive protein
The c-substance is present in some bacteria (the poly saccharides that are at the surface (antigen) as part of the glycoprotein on pneumococci and other bacteria

So it is a biomarker in cases of tissue injury , infection, inflammation .

Alpha-1-antiproteinase :

It's the same as alpha-1 antitrypsin , it inhibits trypsin there fore there will be activation for the elastase which degrades the elastin fibers , especially the ones in the lung which will lead to emphysema
It is a middle size glycoprotein 52 kDa

It makes a good percentage in the plasma 90%
It's a serine protease inhibitor